UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ELI SPORN, Individually and on behalf of all others similarly situated, Plaintiff, v. BRAINSTORM CELL THERAPEUTICS INC., CHAIM LEBOVITS, STACY LINDBORG, and RALPH KERN Defendants.	**Case No: 1:23-cv-09630-DEH** **AMENDED CLASS ACTION COMPLAINT FOR VIOLATIONS OF THE FEDERAL SECURITIES LAWS** JURY TRIAL DEMANDED CLASS ACTION

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NATURE OF THE ACTION

1. Lead Plaintiff George Colby and named Plaintiffs Eli Sporn and Brett Shirley ("Plaintiffs" or "Investors"), individually and on behalf of all others similarly situated, allege the following based upon personal knowledge as to Investors' own acts and upon information and belief as to all other matters based on the investigation conducted by and through Investors' attorneys. This investigation included, among other things: review and analysis of U.S. Securities and Exchange Commission ("SEC") filings by Brainstorm Cell Therapeutics, Inc. ("Brainstorm" or the "Company"); Brainstorm's press releases and earnings call transcripts; public information regarding Brainstorm including information on Brainstorm's website; analyst reports and media reports about Brainstorm; documents publicly available on the Food and Drug Administration ("FDA") website concerning Brainstorm's Biologics License Application ("BLA") 125782, including the FDA Briefing Document issued on September 25, 2023 ("Briefing Document")[1] and the September 27, 2023 Transcript from the FDA Center for Biologics Evaluation and Research (CBER) 75th Meeting of the Cellular, Tissue, and Gene Therapies (CTGR) Advisory Committee ("AdComm Meeting Transcript")[2]; and interviews with former employees of Brainstorm. Investors believe that substantial evidentiary support will exist for the allegations set forth herein after a reasonable opportunity for discovery.

2. Investors bring this securities class action on behalf of all persons or entities who purchased publicly traded Brainstorm common stock during the period February 18, 2020 through September 27, 2023, inclusive, and who were damaged thereby (the "Class Period"). Investors seek to recover compensable damages caused by Defendants' violations of the federal securities

[1] A copy of FDA Briefing Document is annexed hereto as Exhibit A.
[2] A copy of the AdComm Meeting Transcript is annexed hereto as Exhibit B.

laws under the Securities Exchange Act of 1934 (the "Exchange Act"). The action charges that the defendants named herein violated 10(b) and 20(a) of the Exchange Act, and Rule 10b-5 promulgated thereunder by the U.S. Securities and Exchange Commission.

PRELIMINARY STATEMENT

3. Brainstorm is a clinical-stage biopharmaceutical company that has billed its proprietary stem-cell product, "NurOwn", as a potential treatment for a host of neurodegenerative and neurological disorders from Alzhiemeimer's to Autism. This action concerns Brainstorm's efforts to commercialize NurOwn to treat Amyotrophic Lateral Sclerosis ("ALS"), also known as Lou Gehrig's disease. ALS is an incurable and ultimately fatal disease that causes decline in all areas of motor functioning.

4. After conducting a Phase 2 trial of NurOwn, Brainstorm began meeting with FDA in November 2016 to discuss the results of the Phase 2 trial and the Company's design of its Phase 3 trial. Brainstorm intended to use the results of the Phase 3 trial (the "Phase 3 Trial" or "Trial") to obtain FDA approval to market NurOwn to treat ALS.

5. According to Brainstorm's former Global Head of Regulatory Affairs, Brainstorm's CEO, Chaim Lebovitz, communicated directly with FDA and attended FDA meetings, essentially usurping the role of the Company's Head of Regulatory Affairs.

6. Brainstorm determined that the primary efficacy endpoint of the Phase 3 Trial should be the rate of change in participants' ALS Functional Rating Scale ("ALSFRS") scores. The ALSFRS is a rating scale that measures an ALS patient's functional decline in various areas of motor functioning.

7. As to the Phase 3 Trial's patient population, Brainstorm determined it would enroll only "rapid progressors" in the Phase 3 Trial. Brainstorm made this determination based on an

exploratory subgroup analysis of the Phase 2 trial results which purportedly showed that "rapid progressors" treated with NurOwn (who had more severe ALS) showed better results than "slow progressors."

8. Brainstorm met with FDA on November 21, 2016, August 7, 2017, November 8, 2019, and February 5, 2020.

9. At these meetings, FDA stated numerous times that it disagreed with Brainstorm's proposed primary efficacy endpoint for the Phase 3 Trial. FDA additionally recommended that Brainstorm obtain an SPA- a formal agreement with FDA concerning the trial design that ensures alignment between the company and FDA on design and protocol- for the Trial[3].

10. As to Brainstorm's proposal to enroll only "rapid progressors" in the Phase 3 Trial FDA told Brainstorm that it should not enroll only "rapid progressors" because Brainstorm's subgroup analysis suggesting benefit to rapid progressors correspondingly suggested harm to slow progressors. FDA stated, "these inconsistent effects are most likely spurious." In other words, it made no sense that a product that supposedly had "neuroprotective" effects would benefit those with advanced ALS (i.e. "rapid progressors") but *harm* patients with mild ALS (i.e. "slow progressors"). Brainstorm derived this hypothesis from exploratory *post hoc* subgroup analyses of the data from its Phase 2 Trial. But as FDA told Brainstorm at the November 8, 2019 meeting, these subgroup results "do not support that your product has any meaningful activity in the treatment of ALS" and "are most likely spurious and misleading, as if often the case for subgroup analyses."

[3] SPA stands for Special Protocol Assessment. SPA is a process where the trial sponsor and FDA discuss the design and size of a clinical study to determine if it adequately addresses scientific and regulatory requirements that could support marketing approval. An SPA agreement indicates FDA's concurrence with the adequacy and acceptability of the specific elements of the overall trial protocol design. *FDA Guidance for Industry Special Protocol Assessment* (2018).

11. Nonetheless, in contravention of FDA's explicit advice, Brainstorm enrolled only "rapid progressors" in the Phase 3 Trial despite FDA telling Brainstorm doing so was not scientifically justified; did not obtain an SPA with FDA; and utilized a primary efficacy endpoint it knew FDA disagreed with. Because Brainstorm enrolled only "rapid progressors" in the Phase Trial, the Phase Trial population was skewed towards individuals with more severe ALS and did not have a balanced patient population. This contravened both FDA's explicit advice and published FDA Guidance on conducting trials for potential ALS treatments which stated that trial sponsors should not unnecessarily exclude patients from trial enrollment based on disease stage.

12. Despite this, Brainstorm and its senior executives represented to investors that the Phase 3 Trial was "aligned with current FDA views," and that FDA "commented that this is a well-designed trial." Defendants concealed all the FDA's above admonitions.

13. On November 17, 2020, before the market opened, Brainstorm announced top-line results from the Phase 3 Trial. The Phase 3 Trial failed to reach statistical significance on its primary endpoint, though Defendants claimed it showed "numerical improvements" across primary and secondary efficacy endpoints. On this news, Brainstorm's stock price declined $7.88 per share, or 66% from the previous day's closing price of $11.90/share to close at $4.02.

14. While continuing to conceal FDA's advice regarding the Phase 3 Trial's design, Defendants represented that the Phase 3 Trial "included a more severely affected ALS population," and stated, "we identified a superior treatment response in a ***pre-specified*** subgroup of patients with less advanced disease." Defendants told investors they were in active discussions with FDA, who committed to prioritizing review of the data.

15. The purportedly "pre-specified" subgroup consisted of patients with ALSFRS-R scores of 35 or above, patients with mild ALS. The subgroup of patients with ALSFRS-R scores

of 35 or over was a *post hoc* exploratory analysis, focusing on what is referred to as "floor effect." Bounded scales, such as the ALSFRS-R may be subject to "ceiling" or "floor" effects, where the scale cannot detect further deterioration (or improvement) of function. Once an item on the ASLFRS-R reaches zero, a further decline in function cannot be measured, which can make a treatment effect difficult to measure in patients with low ALSFRS-R scores. Defendants conjectured that the lack of efficacy in the Phase 3 Trial overall was due to the inability to detect efficacy in a subgroup that was supposedly impacted by "floor effect."

16. Unbeknownst to Investors, this subgroup was not pre-specified. As FDA stated, "***pre-specification is the cornerstone of reliable regulatory evidence…Without a prespecified hypothesis testing strategy [this subgroup] is an exploratory analysis…[which] cannot be used to rescue the trial because of a large chance of a false positive finding.***"[4]

17. Essentially, Brainstorm's failure to follow FDA's advice concerning the Phase 3 Trial design and enroll "rapid progressors" - patients with more advanced ALS - enabled Defendants to manipulate the Trial in a way that would generate misleading false positive results to support a claim of efficacy. Defendants tried to rescue the failed Phase 3 Trial through *post hoc* subgroup analysis by claiming that the Phase 3 Trial would have succeeded but for the fact that the Trial population consisted of patients with more advanced ALS who "fell victim to the floor effect." Defendants excluded nearly ***50%*** of the Phase 3 Trial data on the pretext of "floor effect."

18. On February 21, 2021 the Company had a teleconference with FDA. First, FDA told the Company it interpreted the Phase 3 Trial as a negative trial, that submission of a BLA was not appropriate, and that the data did not meet the standard required for approval. Second, FDA discredited Brainstorm's "floor effect" analysis, stating the "suggested 'floor effect' did not appear

[4] All emphasis is added unless stated otherwise.

consistent across the study population." Third, FDA stated that if Brainstorm wishes to continue developing NurOwn as a potential treatment for ALS it should "***conduct another Phase 3 study this time incorporating Agency input regarding the study design.***" Fourth, FDA stated it "***remains concerned about the larger number of deaths among subjects treated with [NurOwn] compared to that among subjects treated with placebo.***" Indeed, there were over three times more deaths in the treatment group compared to the placebo group.

19. On February 22, 2021, prior to market open, Brainstorm issued a press release informing investors that FDA "concluded from their initial review [of the Phase 3 Trial data] that the current level of clinical data does not provide the threshold of substantial evidence that FDA is seeking to support a [BLA]. In addition, FDA advised that this recommendation does not preclude Brainstorm from submitting a BLA submission." Brainstorm stated in the press release that it would consult with experts, regulatory advisors, and others before making a final decision as to whether to submit a BLA to FDA.

20. On this news, Brainstorm fell $2.70/share, a 39% decline, from its closing price of $6.90 on February 19 (the previous trading day) to open at $4.20 on February 23, 2021.

21. Despite the bad news, Defendants concealed FDA's concern about the number of deaths in the Phase 3 Trial's treatment group, the existence of the deaths themselves, FDA's invalidation of Brainstorm's "floor effect" analysis, FDA's recommendation that Brainstorm conduct a new trial that (unlike the Phase 3 Trial) followed the FDA's advice concerning trial design, and left open the possibility of submitting a BLA.

22. Then, after remaining tight-lipped about a potential BLA for approximately 18 months, on August 15, 2022, Brainstorm announced that it would submit a BLA for NurOwn to FDA. Defendants represented that a "correction" in the statistical analysis of the Phase 3 Trial data

resulted in one of the "key" ***prespecified*** secondary endpoints reaching statistical significance-again referring to the "***prespecified efficacy subgroup of participants with a baseline score of at least 35***."

23. Defendants emphasized that this analysis carried a "***different level of credence"*** because it was a ***"prespecified threshold."*** Defendants further noted that "***efficacy subgroup analyses play an important role in the evaluation of NurOwn's treatment effect because of the higher number of participants enrolled in this clinical trial with advanced ALS at baseline,"*** continuing to conceal that FDA explicitly told the Company not to enroll a patient population skewed toward "advanced ALS at baseline."

24. In touting the submission of a BLA Brainstorm also highlighted new biomarker analyses from the Phase 3 Trial. In ALS, a reduction in a biomarker called Neurofilament Light, or NfL is thought to be associated with a reduction in neurodegeneration, and so is considered positive. However, in Brainstorm's Phase 3 Trial, a reduction in NfL correlated with a ***worse*** clinical efficacy outcome, ***the opposite of what would be expected*** and an undesired result. Despite this, Defendants touted the biomarker data as "going in the direction that we expected with NurOwn and stability."

25. On September 9, 2022 the Company submitted the BLA to FDA.

26. On November 10, 2022 the Company issued a press release informing investors that the FDA issued a RTF or "refusal to file," the BLA. In response to news of the RTF, Brainstorm's share price fell $1.22 per share, or 42.21%, to close at $1.67 per share on November 10, 2022.

27. In disclosing FDA's RTF, Brainstorm stated only that the RTF "included *one item* related to the trial not meeting the standard for substantial evidence of effectiveness and Chemistry, Manufacturing and Controls ("CMC") related items."

28. Unbeknownst to Investors, in the RTF letter FDA informed Brainstorm, among other

things, that the BLA submission was "***scientifically incomplete to demonstrate substantial evidence of effectiveness, and that the manufacturing information was grossly deficient to ensure product quality***." The RTF further detailed the multitude of "critical information" not provided in the BLA, including "missing or inadequate control materials", "validation of methods missing or incomplete", "lack of data demonstrating manufacturing consistency", "control strategy for prefilled syringe not provided", "inadequate testing and facility information", and "facilities not ready for inspection."

29. Former high-level employees at Brainstorm who reported directly to the Individual Defendants (defined below) confirmed that Defendants "didn't want anybody to know" about the contents of the RTF and refused to let them see it. These senior employees noted that this secrecy was "highly unusual and frustrating" given that the RTF was directly relevant to these employees' job functions.

30. After announcing the RTF Defendants downplayed its contents, represented that the deficiencies in the BLA were "easily fixable," that the CMC issues were "trivial", and continued to tout NurOwn's safety and efficacy and its prospects for FDA approval. Defendants also continued to tout the Phase 3 Trial's "positive" biomarker results and the importance of the results from the "pre-specified" subgroup of patients not impacted by the "floor effect."

31. On January 11, 2023 the Company had a meeting with FDA to discuss the deficiencies identified in the RTF. One week prior to the meeting Brainstorm's Chief Medical Officer, Ralph Kern, resigned.

32. At the January 11, 2023 meeting FDA definitively informed Defendants, in response to their "floor effect" analysis that ***the lack of efficacy of NurOwn over placebo cannot be explained by a floor effect…these findings from the exploratory subgroup analysis can only be used for hypothesis generation, not as evidence of effectiveness to support approval."*** FDA

presented Brainstorm with two options: submit a new BLA with evidence of safety and efficacy from new adequate and well-controlled clinical investigations, or request that the BLA be filed over protest.

33. On March 27, 2023, Brainstorm issued a press release informing investors that it filed the BLA using the file over protest procedure, as well as "filed an amendment to the BLA which responds to most of the outstanding questions the FDA has posed." Defendants represented that the Phase 3 Trial had "***fewer deaths than we expected. We have a very strong safety profile***." Defendants also stated that at the January 11 meeting FDA provided them with "***multiple options to return the BLA to regulatory review***" and that "there was no downside utilizing the File Over Protest pathway."

34. Because Defendants continued to emphasize the critical nature of the "pre-specified" subgroup of patients with ALSFRS scores of over 35 given their explanation that the Phase 3 Trial's failure to reach its primary endpoint was "very likely driven by participants who entered the trial with advanced ALS, who fell victim to the floor effect of the ALS functional rating scale," one analyst asked "how FDA feels about the floor effect…do they understand the impact that it can have at trials like yours?" Brainstorm's co-CEO Stacy Lindborg responded "***"the FDA has certainly seen this data and clearly and has not disagreed with the statements we made."***

35. As to CMC, Defendants represented that the Company's amendment to the BLA "responds to the majority of the manufacturing items raised in the [RTF]", that "we have conducted much of the work necessary in a short time frame" and touted Brainstorm's "exemplary record of high-quality manufacturing."

36. On September 25, 2023, ahead of the FDA Advisory Committee Meeting, FDA released the Briefing Document. On September 27, 2023 the Advisory Committee meeting took

place as planned. The Advisory Committee Members voted 17:1 against FDA approval of NurOwn.

37. Defendant Lindborg represented the Company at the AdComm Meeting. Lindborg herself admitted at the Meeting, when asked about CMC deficiencies, "***we acknowledge that additional work needs to be done and complete to fully satisfy the FDA requirements***."

38. The FDA Briefing Document and FDA Panelist's comments at the Advisory Committee Meeting fully revealed the truth concerning Defendants' prior misrepresentations about Phase 3 Trial's design and results, and the Company's interactions with the FDA, among other things. For example, the Briefing Document and Advisory Committee transcript revealed:

- ***Survival in the Phase 3 study was worse at study completion for subjects who received [NurOwn]. A total of 13 deaths occurred during the post-treatment follow up with 10 deaths in the [NurOwn] group and 3 deaths in the placebo group.***

- ***Particularly concerning was the larger number of deaths in the [NurOwn] group compared to the placebo group…***

- ***FDA and applicant did not reach agreement on the primary efficacy endpoint for the Phase III study.***

- ***The Phase Two study failed to show a statistically significant benefit of [NurOwn] for treatment of ALS. However, the applicant conducted an exploratory subgroup analysis of rapid progressors versus slow progressors….FDA communicated to the applicant concerns about the definition of rapid progressors and the exploratory nature of the subgroup findings. However, for the Phase Three study, the applicant then selected only patients who appear to be rapid progressors.***

- ***[NurOwn] showed no efficacy compared to placebo on primary and all key secondary endpoints in the overall population. BCT-002-US [The Phase 3 Study] was a failed study. The applicant then tried to rescue the failed study by exploring various subgroups. However, we reiterate the statistical principle that exploratory and post hoc subgroup analysis cannot provide substantial evidence of effectiveness to support regulatory approval because such analysis has a high risk of obtaining false positive results.***

- ***The Applicant states that these sub-group analyses were "pre-specified." However, it is important to note that these subgroup analyses were not***

prespecified ***for hypothesis testing and no prespecified multiplicity adjustment strategy was employed. Subgroup tests following overall nonsignificant tests in the population as a whole such as the Phase 3 study can only be considered exploratory and hypothesis- generating and do not constitute evidence of effectiveness to support marketing approval of [NurOwn].***

- ***…Prespecification is the cornerstone of reliable regulatory evidence. Without a prespecified multiple hypothesis testing strategy, the subgroup analysis of patients with baseline ALSFRS-R score greater than or equal to 35 is an exploratory analysis.*** **In the presence of an overall negative trial result, this subgroup analysis may be used to generate a hypothesis for another trial.** ***However, they cannot be used to rescue the trial because of a large chance of a false positive finding***

- ***The applicant's biomarker analyses were exploratory and did not support clinical benefit….. [ ] a reduction in NfL is expected to be associated with reduction in clinical decline of ALSFRS-R total score. However, in the current data set, patients experiencing greater loss of function appear to have a higher reduction of NfL, the opposite of what would be expected.***

- ***[I]t is not appropriate to combine non-significant results into a significant trend because the more comparisons you make, the more likely one of them would have been statistically significant. But in this case, none of them were. Perhaps most importantly, more patients taking the treatment died.***

39. When FDA released the Briefing Document on September 25, 2023 Brainstorm common stock fell $0.39/share, or 48% from its closing price $0.82 on September 22, 2023 (the previous trading day), to close at $0.43 on September 25, 2023, damaging investors.

40. News of the AdComm Meeting results two days later caused Brainstorm's stock price to decline further, by another 48.72%, or $0.19 per share, to close at $0.20 per share on September 28, 2023.

41. During the Class Period Brainstorm sold over $73 million in common stock to investors in a series of At-the-Market (ATM) Offerings, capitalizing on the artificially inflated share prices resulting from Defendants' fraud. For example, in one such offering Brainstorm sold close to one million shares of stock at a price of $14.48 per share for proceeds of $13.71 million. By the end of the Class Period these shares were worth a total of only $189,525.

42. Similarly, Brainstorm's CEO sold nearly $1 million worth of his Company stock during the Class Period at prices between $12.99 and $13.47 per share. At the end of the Class Period these shares were worth a meager $14,350.60.

JURISDICTION AND VENUE

43. The claims asserted herein arise under and pursuant to Sections 10(b) and 20(a) of the Exchange Act (15 U.S.C. §§ 78j(b) and 78t(a)) and Rule 10b-5 promulgated thereunder by the SEC (17 C.F.R. § 240.10b-5).

44. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1331, and Section 27 of the Exchange Act (15 U.S.C. §78aa).

45. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391(b) and Section 27 of the Exchange Act (15 U.S.C. § 78aa(c)) as the alleged misstatements entered and the subsequent damages took place in this judicial district.

46. In connection with the acts, conduct and other wrongs alleged in this complaint, Defendants (defined below), directly or indirectly, used the means and instrumentalities of interstate commerce, including but not limited to, the United States mails, interstate telephone communications and the facilities of the national securities exchange.

PARTIES

47. Lead Plaintiff George Colby purchased Brainstorm common stock at artificially inflated prices and suffered damages as a result of the federal securities law violations alleged herein. Mr. Colby's updated PSLRA Certification is attached hereto as Exhibit C.

48. Named Plaintiff Brett Shirley purchased Brainstorm common stock at artificially inflated prices and suffered damages as a result of the federal securities law violations alleged herein. Mr. Shirley's PSLRA Certification is attached hereto as Exhibit D.

49. Named Plaintiff Eli Sporn, (as set forth in his PSLRA Certification filed with the Court in connection with the initial complaint in the Action (ECF No. 1-1)) purchased Brainstorm common stock at artificially inflated prices and suffered damages as a result of the federal securities law violations alleged herein.

50. Defendant Brainstorm is a Delaware corporation with its principal office located at 1325 Avenue of Americas, 28th Floor, New York, New York, 10019. Brainstorm common stock trades on the Nasdaq Stock Market ("NASDAQ") under the ticker symbol "BCLI."

51. Brainstorm described itself in its Class Period 10-K's as a "leading biotechnology company committed to the development and commercialization of best-in-class autologous cellular therapies for the treatment of neurodegenerative diseases…" Despite characterizing itself as a "leading" biotech, Brainstorm has operated at a loss since its inception, and has consistently warned investors that it may not be able to continue as a going concern if it does not raise sufficient capital. Brainstorm has no products on the market. Brainstorm's development processes are subject to FDA approval and oversight.

52. Defendant Chaim Lebovits ("Lebovits") is the President and Co-Chief Executive Officer of Brainstorm. Lebovitz joined Brainstorm in 2007. Prior to joining Brainstorm, Lebovitz's business involved gold and diamond mining in the Democratic Republic of the Congo. Lebovitz had actual knowledge and supervision over Brainstorm's communications with FDA and the true (undislosed) facts concerning the Company's clinical trial results, BLA submission, and FDA approval process. For example, Lebovits attended the Company's face-to-face meetings with FDA concerning its clinical development of NurOwn to treat ALS, communicated directly with FDA concerning the clinical development of NurOwn on behalf of Brainstorm, and received a copy of the RTF.

53. Non-party AAC Holdings, International ("AAC Holdings") is an investment company owned and controlled by Defendant Lebovitz. According to Brainstorm's Class Period SEC filings, Defendant Lebovitz is the beneficial owner of the Brainstorm stock held by ACC Holdings. During the Class Period Defendant Lebovitz owned as much as 16% of Brainstorm's common stock through AAC Holdings and other related entities, in addition to shares personally held.

54. Defendant Stacy Lindborg ("Lindborg") has served as the Company's Co-CEO since January 3, 2023. From June 2020 to January 2023 Lindborg served as the Company's Executive Vice President and Chief Development Officer. Lindborg had actual knowledge and supervision over Brainstorm's communications with FDA and the true (undislosed) facts concerning the BLA submission and FDA approval process. Lindborg delivered Brainstorm's presentation at the September 27, 2023 FDA Advisory Committee Meeting. According to Defendants, Lindborg served at the overall leader for Brainstorm's entire BLA process for NurOwn and was "a key driver of analytics and insights gained from the phase III trial" and "authored key non-clinical and clinical modules of the BLA." Lindborg received a copy of the RTF. In addition, Lindborg is a medical statistician.

55. Defendant Ralph Kern served as Brainstorm's President and Chief Medical Officer ("CMO") from April 2020 through January 3, 2023. Prior to that Kern served as the Company's Chief Operating Officer (from March 2017 until April 2020). When Kern resigned as CMO in January 2023 he became a member of the Company's Scientific Advisory Board, which advises management on scientific matters such as research, clinical trials, and drug development. Kern had actual knowledge and supervision over Brainstorm's communications with FDA and the true (undislosed) facts concerning the BLA submission and FDA approval process. For example, Kern

presented results from the Company's Phase 3 Study of NurOwn at numerous conferences during the Class Period and received a copy of the RTF.

56. Defendants Lebovits, Lindborg, and Kern are collectively referred to herein as the "Individual Defendants."

57. Each of the Individual Defendants, because of their positions with the Company, possessed the power and authority to control the contents of the Company's reports to the SEC, press releases and presentations to securities analysts, money and portfolio managers and institutional investors, ***i.e.,*** the market. The Individual Defendants were provided with copies of the Company's reports and press releases alleged herein to be misleading prior to, or shortly after, their issuance and had the ability and opportunity to prevent their issuance or cause them to be corrected. Because of their positions and access to material nonpublic information available to them, the Individual Defendants knew that the adverse facts specified herein had not been disclosed to, and were being concealed from, the public, and that the positive representations which were being made were then materially false and/or misleading. The Individual Defendants are liable for the false statements pleaded herein.

58. Defendant Brainstorm and the Individual Defendants, are collectively referred to herein as "Defendants."

DEFENDANTS' MISCONDUCT

I. BACKGROUND

ALS and NurOwn

59. ALS is a progressive, and ultimately fatal, neurodegenerative disease that primarily affects motor neurons in the cerebral motor cortex, brainstem, and spinal cord, leading to loss of voluntary movement and difficulty swallowing, speaking, and breathing. There is no known cause

for ALS, though a small minority of patients have a family history of ALS.

60. While ALS is a heterogenous disease, all forms of the disease are marked by degeneration of both upper and lower motor neurons. Most patients die within three to five years of onset. Only 10% of ALS patients survive more than ten years.

61. There are few approved treatments for ALS, and none that reverse the damage to motor neurons ALS causes. The benefits of approved treatments for ALS are modest. In 1995, FDA approved the first drug to treat ALS, called Riluzole. In clinical trials, Riluzole prolonged survival in some patients by 2-3 months. In 2017, FDA approved Edaravone, a medication given orally or intravenously, that has been shown to slow functional decline in some ALS patients. More recently, in September 2022 the FDA approved Relyvrio, manufactured by Amylyx, which was also shown to slow functional decline. On April 25, 2023, FDA approved Biogen's drug Tofersen, which is given through a spinal injection to ALS patients that have a mutation in the SOD1 gene.

62. Brainstorm's lead product candidate, Debamestrocel ("NurOwn" or "MSC-NTF") is a cellular therapy composed of mesenchymal stromal cells, also referred to as mesenchymal stem cells (MSCs). MSCs are adults stem cells traditionally found in the bone marrow. NurOwn is an autologous product (meaning it comes from stem cells of the patient itself) generated from a single bone marrow aspirate. The manufacturing process is intended to increase the levels of neurotrophic factors (NTFs) normally produced by MSC to generate a cellular product. Brainstorm refers to this cellular product as "MSC-NTF" cells. NurOwn is intended to work through the secretion of MSC-NTF factors that purportedly "modulate neuroinflammatory and neurodegenerative disease processes, promote neuronal survival and improve neurological function." NurOwn is administered into a patient's cerebrospinal fluid through a standard

injection.

FDA Regulatory Background

63. In the United States, FDA regulates biologics under the Federal Food, Drug and Cosmetic Act, of FDCA. NurOwn must be approved by the FDA through the Biologics License Application ("BLA") process before it can be legally marketed.

64. The data necessary to support a BLA is generated in two distinct stages: pre-clinical and clinical. The pre-clinical development stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate pharmacological activity and toxicity in animals, which support subsequent clinical testing. The clinical stage of development involves the administration of the product candidate to healthy volunteers and patients under the supervision of qualified investigators.

65. Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase I, Phase II and Phase III clinical trials. Phase III clinical trials generally involve large numbers of patients at multiple sites, in multiple countries (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of a BLA.

66. After clinical trials, the next step toward FDA approval is to submit a BLA with the agency, which includes clinical trial data and other information. BLA's are designed to provide documentation that product candidate demonstrates the safety and efficacy of the drug.

67. As part of the safety and efficacy data, the company provides information regarding

the chemistry, manufacturing and control ("CMC") of the product candidate. The CMC includes information about the manufacturing process, facilities that will be used to ensure product quality, and results of analytical testing conducted on the chemistry of the product candidate.

68. The critical elements of CMC look at: how and where the drug is made, how raw materials are tested and monitored, what control procedures are in place to assure product consistency and quality, whether quality attributes are adequately identified and characterized for the product, whether test methods to use product quality are appropriate, and how long the product maintains its quality after it is made.[5] CMC exists to assure that the drug sold to the public will have quality attributes similar to those of the drug demonstrated to be safe and effective; to assure that the quality of the drug meets appropriate standards and is consistent; and to assure that the drug is the same drug as described on the label. In short, CMC helps maintain the connection in quality between the drug used in the clinical studies and the drug to be marketed to consumers. For example, a manufacturing process under control will exhibit consistency of product quality with low variability between different batches of the product.

69. Under the Public Health Services Act ("PHS") a biological product such as NurOwn cannot be licensed by the FDA unless the company demonstrates that it is "safe, pure, and potent." 42 U.S.C. § 262(a)(2)(C)(i)(I).

70. FDA's implementing regulations interpret the term "potency" to include "effectiveness." See 21 C.F.R. § 600.3(s). Accordingly, FDA has "generally considered substantial evidence of effectiveness to be necessary to support licensure of a biological product under section

[5] *See* "Chemistry, Manufacturing and Controls (CMC) and Good Manufacturing Practices (GMPs): The Big Picture of a Long-term Commitment," Elizabeth Pollina Cormier, Ph.D., Review Chemist Division of Manufacturing Technologies FDA/CVM/ONADE, available at: www.accessdata.fda.gov>static>cvm>cormier>CMCsandCGMPS.

351 of the PHS Act." FDA, Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products [Draft], pp. 3-4 (Dec. 2019) ("Substantial Evidence Draft Guidance").

71. The "substantial evidence" of effectiveness standard refers to both the quality and quantity of the evidence provided. 21 U.S.C. § 355(d). With respect to quality, FDA typically requires sponsors to demonstrate effectiveness via "adequate and well-controlled" clinical investigations, *i.e.* clinical trials. 21 U.S.C. § 355(d). "Reports of adequate and well-controlled investigations provide the primary basis for determining whether there is 'substantial evidence' to support the claims of effectiveness for new drugs[,]" including biological products. 21 C.F.R. § 314.126(a).

72. The FDA's statutory standards for effectiveness apply to drugs and biologics used to treat ALS as they do to all other drugs and biologics. The FDA has stated that is appropriate to exercise regulatory flexibility "in applying the statutory standards to treatments for serious diseases with unmet medical needs (like ALS), ***while preserving appropriate assurance of safety and effectiveness."*** *Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment, Guidance for Industry*, September 2019 ("ALS Guidance") at p. 3.

73. The conclusion that a study has demonstrated an effect of a drug or biologic is critical to meet the legal standard, under Section 351 of the Public Health Services Act, for substantial evidence of effectiveness. *Multiple Endpoints in Clinical Trials, Guidance for Industry* Draft Guidance, January 2017, at p. 3).

74. To establish a drug's effectiveness, it is essential to distinguish the effect of the drug from "from other influences, such as spontaneous change in the course of the disease, placebo effect, ***or biased observation***." 21 CFR 314.126.

75. In order to determine whether a proposed treatment has an effect, a sponsor of a clinical study must use the appropriate endpoints.

76. In clinical trials, the statistical analysis plan must be determined before the trial begins and the final determination of efficacy must be made based on the pre-specified clinical endpoints as analyzed in the pre-specified statistical analysis plan ("SAP").

77. The methodology for assessing, measuring and analyzing the endpoint(s) is detailed in the study protocol and SAP. *FDA Guidance Document on Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics Guidance for Industry*, December 2018.

78. The FDA and the applicant should agree prospectively on the study design and the SAP and the applicant should finalize the study design and SAP before initiating the study, to the extent possible. *FDA Guidance Document on Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics Guidance for Industry*, December 2018 at 14.

79. Another potential option with respect to study design is a Special Protocol Assessment ("SPA"). SPA is a process where the trial sponsor and FDA discuss the design and size of a clinical study to determine if it adequately addresses scientific and regulatory requirements that could support marketing approval. An SPA agreement indicates FDA's concurrence with the adequacy and acceptability of the specific elements of the overall trial protocol design. *FDA Guidance for Industry Special Protocol Assessment* (2018).

ALS Clinical Trial Endpoints

80. With respect to effectiveness endpoints in clinical trials for ALS treatments, FDA has stated that in addition to outcome measures developed for ALS, it supports the development of new outcome measures capable of measuring clinically meaningful effects in patients. In general, effectiveness should be established by the demonstration of a treatment effect (*e.g.*, less

decline, stabilization, improvement) on function in daily activities as measured, for example by the ALSFRS-R of similar scales. ALS Guidance p. 5.

81. Historically, the primary endpoint in clinical trials for treatment of ALS was survival. Early clinical ALS rating scales to assess the functional status and abilities of patients were lengthy, and required clinical time and specialized equipment to administer. In the late 1990's, the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) and its revised form, Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R), became the most widely applied rating scale in ALS clinical trials as a primary or secondary outcome measure.

82. The ALSFRS-R is the most widely used measure for assessing functional deficits in patients with ALS in clinical trials.[6] The ALSFRS-R is an accepted primary endpoint measure for Phase 3 ALS clinical trials to monitor functional decline in patients over time, and a critical part of assessing efficacy. Survival is still relevant, and often measured as a secondary endpoint.[7]

83. The ALSFRS-R has twelve items, and assesses current motor disability across four domains: bulbar, fine motor, gross motor, and respiratory. Each item has five ordinal response options ranging from 0 (complete loss of function) to 4 (normal function), with a total score ranging from 0 to 48. Higher scores indicate higher functioning and lower scores indicate lower functioning.

84. Additional efficacy measurements in clinical trials for ALS treatments include Slow Vital Capacity ("SVC"), which measures the maximum amount of air a subject can exhale in a single breath, and Combined Assessment of Function and Survival ("CAFS"), a composite

[6] Briefing Document (Ex. A) at p. 12.
[7] *Qualitative measures that assess functional disability and quality of life in ALS*, Hartmaier, et al., Health Qual Life Outcomes, January 2022. Available at: https://pubmed.ncbi.nlm.nih.gov/35062955/.

endpoint that combines functional status (i.e. the ALS functional rating scale) with overall survival. Because CAFS accounts for patient deaths it ensures that there is no missing data in a trial due to inability to measure ALSFRS-R or SVC due to patient deaths. Indeed, FDA Guidance states that functional endpoints can be confounded by loss of data because of patient deaths. To address this, FDA recommends sponsors use an analysis method that combines function and survival into a single measure. *ALS Guidance*, p. 7.

85. Sponsors of ALS clinical trials should also characterize an effect on mortality because it is important to the consideration of overall safety and effectiveness profiles. If patient function is intended to be assessed by the primary outcome, mortality should also be integrated into the primary outcome by an analysis method combining survival and function (like CAFS). *ALS Guidance* p. 6.

86. Recent ALS clinical trials have also measured biomarkers. Biomarkers, short for "biological markers" are genes, proteins, or other substances found in blood, cerebrospinal fluid (CSF), or in other body fluids or tissues, that are capable of being measured. There is a large body of research on biomarkers and ALS. A few biomarkers have been validated to identify people most at risk of developing ALS, monitoring how the disease is progressing, or assessing the effectiveness of treatments. One commonly studied biomarker in ALS is Neurofilament Light Chain (NfL). Neurofilaments are proteins that are highly specific to neurons. When neurons are damaged or degenerate, neurofilaments are released into the blood and cerebrospinal fluid. NfL is the most studied neurofilament. NfL levels are significantly elevated in people with ALS. However, elevated levels of NfL are also present in many other neurodegenerative diseases, like dementia and multiple sclerosis. NfL is therefore a "nonspecific" biomarker.

87. The importance of NfL as a biomarker in ALS received much attention in April

2023 when FDA approved Tofersen to treat ALS in patients with a mutation in the SOD1 gene. In approving Tofersen, an FDA advisory committee concluded that a reduction in NfL levels in the Tofersen trial indicated a change on the course of the disease for patients receiving Tofersen, which could then translate over time into benefits like longer life, increased muscle function, and slower disease progression.

88. A reduction in NfL is expected to be associated with a reduction in clinical decline in patients with ALS.[8] Accordingly, a reduction in NfL accompanied with an *increase* in functional decline in a patient means that the NfL measurement decidedly does *not* correlate with efficacy.

The BLA Submission Process

89. When an applicant submits a BLA to FDA, FDA expects the application to be complete to permit a meaningful and complete review of the application. When FDA receives a BLA it performs a filing assessment to make sure the BLA contains all the information necessary to permit a substantive review by the FDA staff. Within 60 days of receipt of the BLA, FDA will either file the BLA or inform the applicant of a refusal to file, or "RTF." Acceptance of the BLA for filing signifies that FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review.[9]

90. On the other hand, if the BLA contains substantive deficiencies or the FDA review team has concerns that cannot be readily rectified, such as absence of effectiveness, FDA can RTF the application. The RTF action also allows an applicant to begin repairing critical deficiencies in the submission sooner than if the deficiencies were identified later, after a complete FDA review of the application.[10]

[8] Advisory Committee Transcript (Ex. B), p. 128.
[9] Ex. A, p. 23.
[10] Ex. A, p. 11.

91. Even if FDA issues an RTF, the applicant may choose to "File Over Protest." In that case, FDA will review the BLA and it may convene an Advisory Committee for additional discussion. With respect to the File Over Protest option, Defendants represented to investors that "despite its name, this mechanism is standard regulatory procedure, and not inherently antagonistic."

92. Throughout the course of a product candidate's development the FDA holds three types of meetings with the sponsor/applicant: Type A, Type B, and Type C. The FDA holds Type A meetings to help advance a stalled product development program, and takes place within 30 days of the FDA receiving a request for a meeting from the applicant. Type B meetings take place within 60 days of a written meeting request and are conducted at specific points in product development: to obtain FDA input prior to submission of an investigational new drug application (pre-IND), certain end of Phase 1 trial meetings, end of Phase 2 and pre-Phase 3 meetings, and prior to submission of a BLA. Type C meetings refer to all other formal meetings regarding the development and review of an investigational product and are scheduled within 75 days of written request.[11]

Relevant Principles of Clinical Trial Design

93. In clinical trials, statistical tests are predefined before the trial begins. *Post hoc* analysis refers to statistical analyses designed and performed after a trial was conducted and the sponsor saw the trial data.

94. A subgroup analysis refers to any evaluation of a treatment effect for a specific endpoint in subgroups of patients identified by baseline characteristics. A researcher sometimes conducts a subgroup analysis to assess treatment effects for a specific patient characteristic. A

[11] Ex. A, p. 54, fn.1.

prespecified subgroup analysis is one that is planned and documented before any examination of the data, preferably in the study protocol itself. A prespecified subgroup analysis will specify the endpoint, the baseline characteristic, and the statistical method used to test for an interaction. [NEJM article]. Prespecification of subgroup analyses provides reassurance against "data dredging." Indeed, ***"[p]respecification is the cornerstone of reliable regulatory evidence."***[12]

95. By contrast, a *post hoc* subgroup analysis is a subgroup analysis where the hypothesis tested is not specified prior to examining the trial data. *Post-hoc* subgroup analyses carry a high risk of finding false positive results for many reasons. Therefore, a hypothesis that is generated by *post hoc* analysis has neither been proven by an experiment nor generated from a scientific basis.

96. For example, in the "Texas Sharpshooter Fallacy," a gunman fires a rifle into a barn, paints a target around the bullet hole, and claims to have hit a bullseye. The fallacy is widely appreciated in the statistics of clinical trials, because the sharpshooter resembles a researcher trying to find statistically significant groups after an experiment is conducted. Data in clinical trials can be sliced in any number of ways, some of which are bound to display statistically significant differences by sheer chance. For example, patients with red hair might have statistically significantly better outcomes. This of course does not mean that having red hair makes a true difference in making the treatment work better.

97. By running multiple *post hoc* analyses, a researcher can all but guarantee a statistically significant result. Just as someone rolling a twenty-sided dice will eventually roll a 20, researchers who run different *post hoc* analyses on the population will eventually find one that shows the treatment "worked." This problem is called "multiplicity" in statistics and results in

[12] Ex. B, p. 123.

inflated false positives.[13]

98. For this reason, experts are skeptical of *post hoc* analyses. As one expert has stated, "Be especially suspicious of investigators highlighting a subgroup treatment effect in a trial with no overall treatment effect. They are usually superfluous subgroup salvages of otherwise indeterminate (negative) trials.[14]" Experts have noted that "*post hoc* observations should be treated with skepticism irrespective of their statistical significance."[15] For this reason, "***exploratory and post hoc subgroup analysis cannot provide substantial evidence of effectiveness to support regulatory approval because such analysis has a high risk of obtaining false positive results.***"[16]

II. Brainstorm's Development of NurOwn: Defendants Ignore FDA's Admonitions and Tell Investors FDA is "Aligned" with Brainstorm's Phase 3 Trial Design

99. Brainstorm's clinical development of NurOwn consists of four clinical trials. The first two were early phase, single-arm trials conducted outside of the U.S. The third trial was a Phase 2 randomized, double blind, placebo-controlled study, BCT-0001-US ("Phase 2 Study") conducted under an FDA Investigational New Drug ("IND") application. The primary endpoint of the Phase 2 Study was safety; secondary endpoints evaluated efficacy. Finally, BCT-002-US was Brainstorm's singular Phase 3, randomized, double-blind placebo-controlled study (the "Trial" or the "Phase 3 Trial").

100. Brainstorm's interactions with the FDA concerning the development of NurOwn began on December 20, 2013, when the Company submitted its IND to FDA. In October 2014,

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[13] Wang R. Statistics in Medicine - Reporting of Subgroup Analyses in Clinical Trials. NEJM 2007; 357;21:2189-2194.
[14] Schulz KF. Epidemiology 5 - Multiplicity in Randomised Trials II: Subgroup and Interim Analyses. Lancet 2005; 354:1657-1661.
[15] Rothwell PM. Treating Individuals 2 - Subgroup Analysis in Randomized Controlled Trials: Importance, Indications, and Interpretation. Lancet 2005; 365:176-86.
[16] Ex. B, p. 123.

FDA granted "Fast Track" designation to NurOwn. Fast track is a process designed the facilitate the development and expedite FDA review of drugs to treat serious conditions and fill an unmet medical need.

101. As stated above, the primary endpoint of Brainstorm's Phase 2 Study of NurOwn (which enrolled 48 patients in three centers in the United States) was safety. The secondary endpoints were efficacy, which Brainstorm chose to evaluate by measuring change in slopes (*i.e.* the rate of change) from the pre-treatment period to post-treatment period in subjects' ALSFRS-R scores between treatment and placebo groups, 12-24 weeks post-treatment.[17] Brainstorm also measured efficacy by looking at the change in slopes in Slow Vital Capacity (SVC) pre-and post-treatment between treatment and placebo groups.

102. As noted above, while the ALSFRS-R is the most widely used efficacy measure, modeling decline on the ALSFRS-R as a linear function- which is what Brainstorm did by looking at the change in slopes- is not accurate. This is because the disease course for individual patients is heterogeneous, and the pace of progression can vary among patients as well as within time periods for an individual patient. It is not uncommon for a patient to have short intervals of plateau or even improvement on the ALSFRS-R.[18]

103. For the Phase 2 Study Brainstorm also conducted an exploratory subgroup analysis of "rapid progressors" versus "slow progressors." Brainstorm defined "rapid progressors" as patients with a decrease in two points or more in ALSFRS-R score from screening to baseline (about 3 months) and "slow progressors" as subjects with a decrease of less than two points in ALSFRS-R from screening to baseline.[19] According to the Company, this subgroup analysis

[17] Ex. A, p. 40.
[18] Ex. A, p. 12.
[19] Ex. A, p. 40-41.

demonstrated that patients in the Phase 2 Study who were rapid progressors benefitted from NurOwn.

104. On November 21, 2016 Brainstorm had a Type B End-of-Phase 2 Meeting with FDA to discuss the Phase 2 Study and to have initial discussions with FDA regarding plans for a Phase 3 trial. Brainstorm's proposed primary efficacy endpoint for the Phase 3 Trial was the proportion of patients whose disease is stabilized or improved as measured by a 1.5 point per month or greater improvement in post-treatment slope versus pre-treatment slope in ALSFRS-R score at 24 weeks from the first treatment.

105. FDA did not agree with Brainstorm's proposed primary efficacy endpoint. At the meeting, FDA explicitly told Brainstorm it ***"strongly recommended that [it] consider a primary efficacy endpoint whose clinical meaningfulness is easier to interpret (e.g., survival; CAFS)."***[20]

106. On August 7, 2017 Brainstorm had a Type C meeting with FDA to discuss the protocol for Phase 3 Trial. At the meeting, FDA expressed concerns to the Company regarding the clinical meaningfulness of defining a "responder" as a patient showing improvement of 1.25 points on more in the slope of ALSFRS-R over time after treatment compared with the slope prior to initiating treatment. FDA once again "***strongly recommended***" to Brainstorm that it instead use either survival or CAFS as the primary efficacy endpoint for the Phase 3 Trial.[21] Further, at the meeting, FDA recommended to Brainstorm that it obtain an SPA for the Phase 3 Trial. *Id.* As stated above, doing so would ensure that the FDA concurred with the Company's trial design and protocol and that the Company and FDA were aligned.

107. In October 2019, Brainstorm completed patient enrollment in the Phase 3 Trial. The

[20] Ex. A, p. 52.
[21] *Id.*

Phase 3 Trial was a randomized, double-blind placebo-controlled trial consisting of 196 patients at various centers in the U.S. who received either three intrathecal injections of NurOwn eight weeks apart, or placebo. Contrary to FDA's admonitions, the Phase 3 Trial evaluated efficacy of NurOwn compared to placebo measured by the proportion of patients with difference in pre-treatment vs. post-treatment slope of ALSFRS-R of 1.25 points or more at 28 weeks. The Phase 3 Trial also evaluated the safety of NurOwn compared to placebo, and measured biomarkers in cerebrospinal fluid (CSF).[22]

108. In the Phase 3 Trial, Brainstorm chose to enroll only "rapid progressors.[23]" Defendants did so ***"despite the FDA's consistent concern about the definition of 'rapid progressors.' And the exploratory nature of the subgroup findings."*** The patients in the Phase 3 Trial had lower ALSFRS-R scores at baseline than the patients in the Phase 2 Study.[24]

109. Brainstorm's decision to enroll only "rapid progressors" also contravened the FDA's ALS Guidance which states:

> ***There is a need to understand the safety and effectiveness of investigational drugs for ALS across disease stages***. Although sponsors may have good reasons to use prognostic enrichment to increase the likelihood of demonstrating a drug effect (*e.g.,* to enroll patients who are more likely to experience rapid progression) or to use predictive enrichment to direct therapy to patients with a particular disease characteristic (*e.g.,* a specific genotype or phenotype), ***sponsors should not unnecessarily exclude patients from trial enrollment based on characteristics such as age or disease stage unless scientifically justified.***[25]

110. Indeed, FDA's statements explicitly informed Defendants that, in the case of the Phase 3 Trial, exclusion of patients based on the "rapid progressors" criteria was *not* "scientifically justified."

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[22] Ex. A, p. 27.
[23] *Id.* p. 43.
[24] *Id.* p. 41.
[25] ALS Guidance, p. 3.

111. On November 18, 2019 Brainstorm had a Type C face-to-face meeting with FDA. Defendants Lebovitz and Kern attended the meeting. At the meeting, FDA officials from FDA's Center for Drug Evaluation and Research (CDER) stated that the Phase 2 study failed to show a statistically significant benefit of treatment with NurOwn compared to placebo. FDA officials stated that while Brainstorm's subgroup analysis suggested benefit to "rapid progressors," that analysis also suggests harm to "slow progressors." FDA stated that these inconsistent effects are most likely spurious.

112. As FDA told Defendants at the November 18, 2019 meeting: "***We interpret your Phase 2 data as evidence that your product is not effective in the treatment of ALS***. ***Your proposal that your Phase 2 data suggest benefit for the 'rapid progressors' is most likely over-interpretation of your subgroup analyses***. In subgroup analyses, the results for the 'slow progressors' could be interpreted to suggest that your product is harmful to some patients with ALS***. However, such subgroup results, for both the 'rapid progressors' and the 'slow progressors', are most likely spurious and misleading, as is often the case for such subgroup analyses.*** We note that it is not clear why a product that you propose to have neuroprotective and immunomodulatory effects would be beneficial for some patients with ALS and harmful to other patients with ALS. Due to their inconsistency (i.e., opposite effects in 'rapid progressors' versus 'slow progressors'), and the unclear biological plausibility for such inconsistency, ***your subgroup results do not support that your product has any meaningful activity in the treatment of ALS.***"[26]

113. Further, as FDA stated in the Meeting Summary of the November 18, 2019 Meeting, which Defendants received several days after the meeting took place, "***[d]espite FDA's consistent concern about the definition of 'rapid progressors' and the exploratory nature of***

[26] Ex. A p. 42.

subgroup findings, the Applicant decided to enroll only 'rapid progressors' in the Phase 3 study."[27]

114. Also at the November 2019 meeting FDA once again expressed disagreement with the Phase 3 Trial's primary efficacy endpoint. However, because the Phase 3 Trial was already underway at the time, FDA told the Company not to modify the existing primary and secondary efficacy endpoints because it was important to maintain the integrity of the ongoing Phase 3 Trial. FDA reasoned that because the Company was collecting survival and joint rank data, the Phase 3 Trial results would still be "interpretable." FDA also again reiterated that the Company should submit a SPA request for a future Phase 3 study ***prior to initiating it***.[28]

115. Then, on February 5, 2020 Defendants Lebovitz, Kern, and other senior Brainstorm executives attend an FDA CBER "Informal Dispute Resolution" meeting to discuss "outstanding issues" including "efficacy endpoints, and analysis of [Brainstorm's] ongoing Phase 3 study." Once again, the FDA stated that it disagreed with the Phase 3 Trial's primary efficacy endpoint. FDA told Defendants that it was committed to reviewing the data once the study was completed, "to determine ***if there is a regulatory path forward that could potentially lead to approval.*** FDA stated that it was willing to review the data prior to formal regulatory submission.[29]

116. Despite that FDA disagreed with the Phase 3 Trial design, on a February 18, 2020 investor conference call Defendants Lebovitz and Kern represented that the Phase 3 Trial was "aligned with FDA views." On the call, Lebovitz gave a "more detailed update on our recent meeting with the FDA, stating: "This meeting was very important and was a watershed moment for our ALS development program…Objectives of this meeting were to confirm that there is a

[27] Ex. A, p. 43.
[28] Ex. A, p. 52.
[29] Ex. A, p. 53.

clear regulatory path forward for NurOwn and ALS." Lebovitz continued, "***We had a wonderful discussion. What was most important to Brainstorm was to confirm the data we are collecting in this Phase 3 trial are aligned with current FDA views when considering a BLA for approval***. At the meeting, the FDA confirmed that the full results of Phase 3 trial is collecting relevant data critical to the assessment of NurOwn's efficacy. ***The FDA also commented that this is a well designed trial***." Lebovitz further represented that the Company could be commercializing NurOwn in 2021, depending on the results of the Phase 3 Trial, stating "***that's why we're so excited that the FDA is having these early conversations about the endpoint, and what they want to gather in the data."***

117. Defendant Kern provided more detail about the meeting, stating "The most important outcome of the discussion, of course, was that ***they confirmed we're completing a well-run study***. It is a very high quality study, and the data that will be collected at the end of this study is relevant and critical to the assessment of NurOwn efficacy. ***It's an important confirmation for us…We obviously were very reassured by their position***."

118. Further, when analyst Jason Kolbert asked Kern about the FDA's views on the Phase 3 Trial endpoint ("if there was any one single endpoint, or if you were to focus in on your FDA discussions…"), Kern pointed to the FDA's recent ALS guidance document (discussed above). Kern stated the recent guidance document was "*one of the reasons why we needed to have a realignment*" and the ALSFRS-R "really forms the foundation for that." While referencing the ALSFRS-R, Kern carefully omitted to disclose that FDA explicitly told the Company it disagreed with a slope-based analysis of the ALSFRS-R in the Phase 3 Trial but that the Company refused to listen to FDA.

119. On March 6, 2020 Brainstorm sold 1,250,000 shares of common stock to investors

in a registered direct offering at a price of $8.00 per share for net proceeds of $10 million. And, during the quarter ended March 31, 2020, Brainstorm sold 336,487 shares of common stock pursuant to an at-the-market (ATM) offering at an average price of $5.32 per share, for gross proceeds of $1.76 million.

120. During the quarter ended June 30, 2020, Brainstorm sold 1,162,527 shares of common stock pursuant to an ATM at an average price of $6.57 per share, raising gross proceeds of approximately $7.64 million.

121. Between July 9, 2020 and July 16, 2020 Defendant Lebovits sold 71,753 shares of Brainstorm stock he beneficially owned through AAC Holdings for proceeds of nearly $1 million ($960,632). Lebovits sold these shares at prices of between $12.99 and $13.47 per share.

122. During the quarter ended September 30, 2020 Brainstorm sold 947,627 shares of common stock pursuant to an ATM at an average price of $14.48 per share raising proceeds of approximately $13.71 million.

123. Then, on November 17, 2020, before the market opened, the Company issued a press release announcing top-line results from the Phase 3 Trial, disclosing that the Phase 3 Trial did not meet statistical significance in its primary efficacy endpoint, although it purportedly showed "numerical improvements" in the treated group compared to placebo across primary and secondary efficacy endpoints. On this news, Brainstorm's stock price fell $7.88 per share, or 66% from the previous day's closing price of $11.90/share to close at $4.02.

124. Despite having failed to reach its primary endpoint, the Company represented that NurOwn demonstrated a "clinically meaningful treatment response" across the primary and key secondary endpoints "***in an important pre-specified subgroup*** with early disease based on ALSFRS-R baseline score ≤ 35." The Company also stated in the press release that "Cerebrospinal

fluid (CSF) biomarker analyses confirmed that treatment with NurOwn resulted in a statistically significant increase of neurotrophic factors and reduction in neurodegenerative and neuroinflammatory biomarkers that was not observed in the placebo treatment group."

125. Defendant Lebovitz represented: "This clinical trial included a more severely affected ALS population compared to other recent ALS clinical trials. ***We identified a superior treatment response in a pre-specified subgroup of patients with less advanced disease***. We are in active discussions with the FDA who have expressed their eagerness to review the data and have committed to prioritize review of this data. Accordingly, investors remained hopeful that the Phase 3 Trial results would support approval of NurOwn despite failing to reach its primary endpoint.

126. Unbeknownst to Investors, the "subgroup" of patients Lebovitz was referring to in the above Press Release was not "pre-specified." As investors would later learn: "***The Applicant states that these sub-group analyses were "pre-specified." However, it is important to note that these subgroup analyses were not prespecified for hypothesis testing and no prespecified multiplicity adjustment strategy was employed***. ***Subgroup tests following overall nonsignificant tests in the population as a whole such as the Phase 3 study can only be considered exploratory and hypothesis-generating and do not constitute evidence of effectiveness to support marketing approval of MSC-NTF.***[30]

127. The subgroup of patients with an ALSFRS-R score of 35 or over was a *post hoc* exploratory analysis, focusing on what is referred to as "floor effect." Bounded scales, such as the ALSFRS-R may be subject to "ceiling" or "floor" effects, where the scale cannot detect further deterioration (or improvement) of function. Once an item on the ASLFRS-R reaches zero, a further decline in function cannot be measured, which can make a treatment effect difficult to

[30] Ex. A, p. 37-38.

measure in patients with low ALSFRS-R ratings. Defendants conjectured that the lack of efficacy in the Phase 3 Trial overall was due to the inability to detect efficacy in a subgroup that was supposedly impacted by "floor effect."

128. During the quarter ended December 31, 2020, Brainstorm sold 3,564,385 shares of Common Stock pursuant to an ATM at an average price of $6.10 per share, raising proceeds of approximately $21.8 million.

129. On February 16, 2021, the Company had a teleconference with FDA CBER leadership to discuss the development of NurOwn to treat ALS. FDA told the Company that it does not consider the Phase 2 Study results to provide evidence of efficacy. FDA stated the Phase 3 Trial did not demonstrate a statistically significant benefit over placebo for the overall Phase 3 Trial population, and that FDA interprets the Phase 3 Trial results as a negative trial. FDA further told Defendants it "does not consider submission of a BLA to be appropriate at this time. ***The available data do not meet the standard required for approval by either the traditional or accelerated pathway. While the applicant has the option of submitting a BLA with existing data, the Agency may refuse to file it. In that event, the Applicant may choose to File Over Protest***."[31]

130. During the February 16, 2021 meeting FDA discredited the Company's "floor effect" analysis stating ***"[Brainstorm's] suggested 'floor effect' did not appear consistent across the study population***. Subjects treated with placebo did not show the same 'floor effect' proposed for subjects who received [NurOwn]. Since the study population was randomized, and the [NurOwn] and placebo group were well-matched, ***a similar floor effect would expect to be present in both groups.***" In other words, FDA informed Defendants that NurOwn's failure to demonstrate

[31] Ex. A, p. 53.

efficacy in the Phase 3 Trial was not due to any supposed "floor effects."[32]

131. At the February 16, 2021 meeting FDA also voiced concern about the alarming number of deaths in the Phase 3 Trial's treatment group. FDA stated it "***remains concerned about the larger number of deaths among subjects treated with [NurOwn] compared to that among subjects treated with placebo.***"

132. Ten patients in the treatment group died, compared to three in the placebo group. Indeed, ***"Survival is the ultimate clinically meaningful outcome measure for a fatal disease like ALS. It is less likely to be affected by variations in assessment.***"[33] In addition, patients in the Phase 3 Trial who received NurOwn had higher numbers of life-threatening serious adverse events (SAEs) and SAEs with fatal outcomes compared to the placebo group, a higher incidence of respiratory failure and dysphagia (swallowing difficulties), and a higher incidence of pain (coccydynia and back pain).[34]

133. At the February 16, 2021 meeting FDA also explicitly told the Company that if it wishes to continue developing NurOwn as a potential treatment for ALS it should "***conduct another Phase 3 study this time incorporating Agency input regarding the study design.***"[35]

134. On February 22, 2021, prior to the market opening, the Company informed investors in a press release only that "FDA concluded from their initial review [of the Phase 3 Trial data the Company submitted] that the current level of clinical data does not provide the threshold of substantial evidence that FDA is seeking to support a [BLA]. In addition, FDA advised that this recommendation does not preclude Brainstorm from submitting a BLA submission." The press

[32] Ex. A, p. 53.
[33] Ex. A, p. 35.
[34] *Id.* p. 51.
[35] Ex. A, p. 53.

release stated that Defendants would consult with experts, regulatory advisors, and others before making a final decision as to whether to submit a BLA to FDA.

135. On this news, Brainstorm fell $2.70/share, a 39% decline, from its closing price of $6.90 on February 19 (the previous trading day) to open at $4.20 on February 23, 2021.

136. Despite the bad news, Defendants concealed FDA's concern about the number of deaths in the Phase 3 Trial's treatment group as well ***as the existence of the deaths themselves***; FDA's invalidation of Brainstorm's "floor effect" analysis and hypothesis that the Phase 3 Trial failed to reach statistical significance because of a subgroup that fell victim to the floor effect; FDA's recommendation that Brainstorm conduct a new trial that (unlike the existing Phase 3 Trial) followed the FDA's advice concerning trial design; and left open the possibility of submitting a BLA, causing Brainstorm's stock price to continue to trade at prices artificially inflated by Defendants' fraud.

137. During the quarter ended March 31, 2021, Brainstorm sold of 1,156,897 shares of Common Stock pursuant to an ATM at an average price of $6.33 per share, raising gross proceeds of approximately $7.3 million.

III. Despite the Failed Phase 3 Trial of NurOwn Brainstorm Claims a "Correction" in the Phase 3 Trial's Data Analysis Shows Efficacy and Announces it will Submit a BLA to FDA

138. Over the next 18 months Defendants remained tight-lipped about a potential BLA submission, telling investors that interactions with the FDA had to remain confidential, and that the Company would determine whether to submit a BLA once it published the results from the Phase 3 Trial. For example, on the Company's November 15, 2021 third quarter 2021 investor conference call, an analyst asked "what is the status of the NurOwn application to the FDA? And will the application be submitted or considered early?" Defendant Lindborg responded: "we've

been clear in our communications[…] before we make a decision around the filing of a BLA application of NurOwn we intended to first publish the results from our trial in a peer-reviewed journal. And second to meet with important members of the ALS community who were not involved in the conduct of our Phase 3 trial. As Chaim [Lebovitz] just shared on this call, we've made great progress with these goals and immediately after the publication is in print, we will be prepared to speak to our plans for filing the BLA."

139. Then, on August 15, 2022 Defendants announced that the Company would submit a BLA for NurOwn to the FDA. Defendants represented that a "correction" in the statistical analysis of the data from the Phase 3 Trial resulted in one of the "key," ***prespecified*** secondary endpoints reaching statistical significance. Defendants explained that this correction "results in a statistically significant treatment difference of more than two points for an important secondary endpoint, average change from baseline in ALSFRS-R, ***in the prespecified efficacy subgroup of participants with a baseline score of at least 35***….***the newly published results…employ the efficacy model as prespecified in the trial's statistical analysis plan…*****"**

140. On an investor conference call the same day, Defendants touted the results from "multiple subgroups" and post hoc analyses as well as biomarker analyses which purportedly correlated with the "clinical outcomes." Defendant Lebovitz stated:

> "While performing routine quality control checks and preparations for upcoming BLA filing, we discovered an error in the statistical model, utilized by a vendor in the analysis of a key secondary endpoint. This is now being corrected... ***Though correcting the error resulted in a change that was relatively small numerically, it does have meaningful positive implications that reinforces and strengthens the conclusions of the Phase 3 study. With the correction, the Phase 3 data are stronger than originally thought as we have achieved statistical significance in a key important secondary endpoints for multiple subgroups, including the trial's pre-specified efficacy subgroup***. The endpoint I'm referring to is average change from baseline to week 28 in ALSFRS-R score in the pre-specified subgroup and trial participants with baseline ALSFRS-R scores of at least 35, which is indicative of patients with less disease progression.

141. According to Defendant Lindborg:

> Although results showed the trial did not reach statistical significance on the primary or secondary endpoints, ***pre-specified*** ***and post hoc analyses showed a larger treatment benefit with NurOwn compared to placebo across both primary and secondary outcomes in patients with less advanced disease***. In addition, data indicate NurOwn had an important effect on a wide range of ***biomarkers*** from all participants in the trial, ***which were shown to be statistically important to the clinical outcomes observed."***

142. Lindborg emphasized the importance of efficacy subgroup analyses in the Phase 3 Trial, supposedly due to the ALSFRS-R floor effect:

> I want to offer one other comment regarding the importance of these analyses, which might not be obvious. ***It's common to pre-specify subgroup analyses in large trials in the industry. However, in this trial, efficacy subgroup analyses play an important role in the evaluation of NurOwn's treatment effect because of the higher number of participants enrolled in this clinical trial with advanced ALS at baseline, which is a distinguishing feature of this trial, compared to other registration trials.***
>
> Given the insensitivity of the ALSFRS-R to measure disease progression in these study participants, ***analyses of trial participants less likely to be impacted by the ALSFRS-R floor effect are critical to the evaluation of NurOwn's treatment effect.*** Subgroup analyses are one strategy to do this. To reiterate a point made earlier, we believe these corrected analyses reinforce and strengthen the conclusion from NurOwn's Phase 3 trial.
>
> …When we look at these subgroups that have just been published and when we look at any of the subgroups, [they are] what are allowing us to understand the treatment effect from this trial ***once we've minimized the effect of the lower end of the ALSFRS-R floor effect…***

143. On the call, analyst Daniel Walker drilled down on Defendant Lindborg's representations concerning ***pre-specified*** secondary endpoints:

> DANIEL WALKER:
>
> And Dr. Lindborg, along those lines, can you please maybe just talk a little more about the ***pre-specified*** secondary endpoint P-values, and how patients and investors should be thinking about these updated P-values?
>
> …So can you maybe just break down the statistics significance of these Phase 3 ***pre-specified*** secondary endpoint P-values that met their endpoint? For

> instance, if you're a patient what should these P-values tell you about NurOwn as a treatment? ***And as an investor, how much confidence should these P-values give you?***

144. In response, Lindborg was careful to emphasize that the subgroup of Phase 3 Trial participants with ALSFRS-R scores of 35 or above was a "***prespecified threshold***" which carries "***a different level of credence***":

> So ***in terms of pre-specified and our endpoints***, our primary and secondary endpoints, it's always really critical that when we're conducting clinical research and this is true in academia, as well as in the industry that we're thinking very carefully about the trial, the questions we want to answer, and then the appropriate ways to analyze the data and really bring forward evidence. ***So your question about pre-specified analyses is important. These were identified before any data was observed in the trial and they therefore give objectivity and a different level of rigor to being able to draw conclusions from the trial. When we look at subgroups, for example, these are also carefully as we focused on the participants that were 35 or above. This was a pre-specified threshold.***
>
> ***So these analyses carry a different level of credence…***

145. Unbeknownst to investors, as the FDA Briefing Document states:

> "***However, it is important to note that these subgroup analyses were not prespecified for hypothesis testing and no prespecified multiplicity adjustment strategy was employed. Subgroup tests following overall nonsignificant tests in the population as a whole such as the Phase 3 study can only be considered exploratory and hypothesis-generating and do not constitute evidence of effectiveness to support marketing approval of [NurOwn].***[36]

146. Further, as the FDA CBER statistical reviewer for the BLA stated at the Advisory Committee Meeting:

> "***Prespecification is the cornerstone of reliable regulatory evidence.*** **Without a prespecified multiple hypothesis testing strategy, the subgroup analysis of patients with baseline ALSFRS-R score greater than or equal to *35 is an exploratory analysis***. In the presence of an overall negative trial result, this subgroup analysis may be used to generate a hypothesis for another trial. ***However, they cannot be used to rescue the trial because of a large chance of a false positive finding.***"[37]

[36] Ex. A, p. 37.

[37] Ex. B, p. 123.

147. Additionally, with respect to the "floor effect," there was in fact no such "floor effect" in the floor effect subgroup, because the patients in the "floor effect" subgroup whose ALSFRS-R scores supposedly could not have declined further, actually had greater declines in scores than the patients in the "no floor effect" subgroup. As the FDA Briefing Document explained:

> FDA did not observe a "floor effect" in the floor effect subgroup defined by any of the three definitions identified by the Applicant. ***If there were a "floor effect" in the Applicant-identified floor effect subgroup, the ALSFRS-R total score post baseline would have been bounded by a "floor," which would have prevented the score from much further decline. This is in direct contrast with the fact that the [NurOwn] "floor effect subgroup" had a drastically steeper decline in ALSFRS-R total score from baseline compared with the no floor effect subgroup or the placebo floor effect subgroup.*** At the same time, the magnitude of change between the placebo floor effect subgroup and the placebo no floor effect subgroup were comparable, which further puts into question the validity of the "floor effect" [ ]. In addition, the [NurOwn] floor effect subgroup showed substantially worse CAFS ranking than the no floor effect subgroups while the two placebo subgroups were comparable Figure 13. ***In conclusion, the lack of efficacy of MSC-NTF over placebo cannot be explained by a floor effect***.[38]

148. Also on the August 15, 2022 investor conference call, Defendants touted new biomarker analyses from the Phase 3 Trial as supporting efficacy and the BLA submission. Defendant Kern stated: I won't give this away today, but what has been true across the board as we work to assess the relationships between biomarker data and clinical endpoints is ***that we consistently see biomarkers that are statistically relevant to clinical endpoints*** covering all these three important ALS pathways. The broad mechanism of action and NurOwn's ability to lower markers of inflammation and neurodegeneration in addition to increasing markers of neuro protection all appear to be important in explaining the clinical response that we have observed.

149. Defendant Lindborg echoed that the biomarker data was consistent with improved clinical outcomes, stating: "***When we look at our biomarker data and we see changes that were***

[38] Ex. A, p. 37-8.

anticipated going in the direction that we expected with NurOwn and stability, which we also expected with placebo and we see very consistent conclusions across the ranges of the scale, the efficacy scale. That again we're very confident in the scale's ability to measure progression. ***We walk away with a set of data that we believe builds on each analysis and allows us to look at look at the trial results in total.***"

150. In truth, the Phase 3 Trial's "positive" biomarker data correlated with ***worse*** clinical outcomes. As the FDA Briefing Document stated: "subjects having higher reduction in CSF NfL level appeared to experience greater loss of function [ ] ***the opposite of what would be expected.***"[39] In other words, "***higher reduction in NfL after [NurOwn] was associated with a worse clinical efficacy outcome***."[40]

151. On September 9, 2022 the Company submitted the BLA to FDA.

152. On November 8, 2022 FDA issued an RTF letter to the Company. The RTF letter "detailed all the deficiencies in the BLA submission and provided the FDA's recommendations on how to resolve the deficiencies."[41] In the RTF letter FDA informed Defendants, among other things, that the BLA submission was "***scientifically incomplete to demonstrate substantial evidence of effectiveness, and that the manufacturing information was grossly deficient to ensure product quality***." "Examples of critical information not provided in the BLA submission include missing or inadequate control materials, validation of methods missing or incomplete, lack of data demonstrating manufacturing consistency, control strategy for prefilled syringe not provided, inadequate testing and facility information, and facilities not ready for inspection."

153. Defendants concealed the contents of the RTF from investors as well as their own

[39] Ex. A, p. 8.
[40] *Id.* p. 47.
[41] Ex. A, p. 27.

employees.

154. Former Employee 1 ("FE1") FE1 served as a Senior Vice President for Medical Affairs and Clinical Innovation at the Company from November 2021 through May 2023. FE1 reported directly to Defendant Kern. After Kern resigned as CMO in January 2023 FE1 began reporting directly to Defendant Lindborg. FE1 stated that Brainstorm's senior leadership was "very secretive." Brainstorm hired FE1 hired to prepare NurOwn for market, but gave FE1 no budget and no money, and Brainstorm had no marketing team, which FE1 described as a "strange, unusual situation" for a company supposedly anticipating receipt of FDA approval to market a product.

155. FE1 asked to see the RTF letter, given that its contents were directly relevant to FE1's job. FE1 was told: "no, you can't see it." FE1 was likewise not permitted access to any of the FDA documents about NurOwn, including FDA correspondence and Brainstorm's amendment to the BLA. FE1 stated that this was highly unusual: "I would understand if it was a large company but it was a small company and I was supposed to be strategizing about how to move forward…It was very weird. I was like, ***'how can we not know? There's something going on.'*** At a large company I could understand that but when it's teeny tiny then your roles are not really well defined. ***They didn't want anybody to know."***

156. Former Employee 2 ("FE2") was a Senior Vice President of Global Strategy and Medical Affairs at the Company from October 2021 to March 2023. FE2 reported directly to Defendant Kern and attended weekly management meetings with Lebovitz, Lindborg, and Kern. FE2 stated that FE2 had no access to any of the FDA documents about NurOwn, including the RTF, the refiled BLA, or the Company's amendment to the BLA. FE2 stated that this lack of access and secrecy was both unusual and frustrating. FE2 stated that this lack of access was "certainly not my choice." FE2 stated, "that was the decision of the CEO [Defendant Lebovitz], the co-CEO

[Defendant Lindborg], and the CMO [Defendant Kern]. The rest of us were not really part of any decision making, even any knowledge about the FDA and Brainstorm as far as what was going on."

157. Former Employee 3 ("FE3") was the Executive Vice President and Global Head of Regulatory Affairs at Brainstorm from September 2020 to February 2021. FE3 reported directly to Defendant Lebovitz and attended weekly meetings concerning NurOwn that Lebovits ran and that all senior executives, including Defendant Kern attended. FE3 stated that as Head of Regulatory Affairs, FE3's job was to communicate with FDA about NurOwn but that instead, Defendant Lebovitz communicated a lot with the FDA himself. FE3 stated that the CEO communicating with FDA when it was FE3's job to do this was unusual and "a dynamic I wasn't comfortable with." FE3 stated "It felt like it was Chaim's way of doing things…You never really felt like you had the whole story. [Lebovitz] played it very close to the vest. I didn't feel like I always knew what was going on." For these reasons, FE3 left the Company.

158. On November 10, 2022, Brainstorm issued a press release informing investors of the RTF. Defendants did not disclose the contents of the RTF, stating the RTF "included *one item* related to the trial not meeting the standard for substantial evidence of effectiveness and Chemistry, Manufacturing and Controls ("CMC") related items."

159. In response to news of the RTF, Brainstorm's share price fell $1.22 per share, or 42.21%, to close at $1.67 per share on November 10, 2022.

IV. Brainstorm Conceals Critical Information Concerning the Substance of the RFT and Files the BLA Over Protest

160. After announcing the RTF Defendants downplayed its contents, represented that the deficiencies in the BLA were "easily fixable," and continued to tout NurOwn's safety and efficacy and its prospects for FDA approval.

161. On November 14, 2022 Brainstorm issued a press release announcing the

Company's request for a Type A meeting with the FDA to "facilitate NurOwn's advancement following receipt of a refusal to file letter regarding the Company's new [BLA]." The press release downplayed the RTF, quoting Lebovitz as stating: "our commitment to ALS patients and our belief in NurOwn's potential to address unmet medical needs remains unchanged, despite our receipt of a refusal to file letter regarding our new [BLA]." The Press Release also highlighted additional analyses that purportedly show that "***after controlling for the impact of the ALSFRS-R floor effect, participants treated with NurOwn had a higher rate of clinical response and less function lost across 28 weeks compared to placebo.***"

162. The press release also emphasized the "new biomarker data" which "provided further evidence confirming NurOwn's multifaceted mechanism of action."

163. On an investor conference call the same day, analyst David Bautz asked Defendant Lebovitz: "I'm curious if you could give just a little bit more information about the CMC issues that the FDA brought up? And perhaps importantly, how costly – how costly- if they will be costly, will those changes need to be? Lebovitz responded: "***So the CMC issues are more trivial issues, it's not really costly. It's asking me some questions about some validation, some others, some are already in the BLA, and we have to point out where it is. Some where we anticipate most of the questions, we receive them as review questions. We don't see outside of the clinical comments any red flags.***

164. On January 4, 2023, just one week shy of the Company's anticipated Type A meeting with FDA to discuss the RTF, Defendant Kern resigned as CMO, without explanation. FE1 stated that Brainstorm employees were told that Kern retired. FE1 was therefore surprised to see that "two months later [Kern] showed up at another job." Indeed, Kern became the Chief Medical Officer of Cognito Therapeutics, Inc. in March 2023.

165. On January 11, 2023 Brainstorm had a Type A meeting with the FDA to discuss the deficiencies identified in the RTF. Brainstorm chose not to discuss the CMC deficiencies despite FDA's concerns about the "gross[ ] deficien[ies] in manufacturing information" and numerous examples of "critical information' on CMC missing from the BLA.

166. At the meeting Defendants presented FDA with Brainstorm's "floor effect" analyses. FDA informed Defendants that "***the lack of efficacy of NurOwn over placebo cannot be explained by a floor effect***" and that "these findings from the exploratory subgroup analysis can only be used for hypothesis generation, not as evidence of effectiveness to support approval."[42]

167. At the January 11 meeting, FDA described the two possible options. The first option was for the Company to "address these clinical and product issues and then submit a new BLA that contains evidence of effectiveness and evidence of safety ***from new adequate and well-controlled clinical investigations*** and describe all the necessary validation studies and document that the applicant's commercial manufacturing facilities were ready for inspection." The second option was to request that the BLA be filed over protest.[43]

168. On February 6, 2023 Brainstorm notified FDA of its request to file the BLA over protest, and re-filed the BLA the next day. On February 9, 2023 the Company received the meeting minutes from the January 11 Type A meeting.

169. In filing the BLA over protest, the Company submitted post-hoc exploratory analysis of the Phase 3 Trial's clinical data, and exploratory analysis of biomarker data, as well as additional CMC information.

170. With respect to the clinical data, Brainstorm performed three different retrospective

[42] Ex. A, p. 37-8.
[43] Ex. A. p. 23.

analyses on an unblinded post-hoc subgroup, excluding patients the Company asserted showed a "floor effect." However, as discussed above, the Company's "floor effect" analysis was flawed and spurious. First, the Company had no solid definition for the "no floor effect subgroup." Instead, Brainstorm used three distinct "no floor effect" subgroups. The fact that one group might show positive findings could simply be due to random chance. *Post hoc* subgroup analyses have a high risk of finding false positives due to many factors. Second, the data demonstrated that NurOwn had a detrimental effect in the "floor effect" subgroups. Third, if there were truly a "floor effect" in the floor effect subgroup, the ALSFRS-S scores of patients in this subgroup would not have declined much further. However the data showed that the "floor effect" subgroup had a drastically steeper decline in ALSFRS-R score from baseline compared to the "no floor effect" subgroup or the placebo group. Accordingly, Defendants had no basis to support their assertion that the lack of efficacy in the overall Phase 3 Trial was due to the subgroup impacted by the "floor effect."[44]

171. With respect to the clinical data, the Company also submitted biomarker data as part to the BLA. However, there was a large amount of missing biomarker data. While Brainstorm collected efficacy data up to week 28 it only collected biomarker data up to week 20. At week 20 up to ***50%*** of the key biomarker data, including NfL, was missing. This degree of missing data compromises the validity of its analysis. Further, the biomarker data was exploratory only because much of the analysis lacked multiplicity adjustment or formal hypothesis testing. Therefore, any claim of statistical significance could simply be due to chance. Finally, the purportedly positive NfL biomarker data, *i.e.* a reduction in NfL (which is associated with neurodegeneration) was seen in subjects with poorer efficacy outcomes.[45]

[44] Ex. A, p. 37-8.
[45] Ex. A, p. 44-9.

172. With respect to safety, as noted above, the data in the BLA showed a higher incidence of death in the NurOwn group, which shows a lack of survival benefit with NurOwn (at the very least), a higher incidence of SAE's, a higher incidence of respiratory failure and difficulty swallowing, and a higher incidence of pain.[46]

173. With respect to CMC, the BLA was missing a large amount of manufacturing information and product data. First, the Company failed to assess, and demonstrate in the BLA, as required, that the product administered was comparable across the studies used to support the BLA and did not even show that the product was comparable in the two different sites that manufactured NurOwn administered in the Phase 3 Trial. Second, the Company did not show that it controlled variability of the product for the Phase 3 Trial. Third, the Company did not validate the product's production process, which is necessary to show that the manufacturing process is consistent. Fourth, one quarter of the doses administered in the Phase 3 Trial did not meet the intended dose requirements. Fifth, the level of NTF production, (i.e., the levels of neurotrophic factors normally produced by MSC to generate NurOwn) was highly variable across the product lots. Sixth, the Company claimed that NurOwn's mechanism of action involved secretion of molecules other than NTF but gave no manufacturing control strategy for any other purported mechanism of action. Relatedly, the Company's proposed mechanism of action in the BLA was inconsistent across the BLA and unclear. Seventh, the product in pre-filled syringes was not necessarily stable and the Company changed a critical reagent used to manufacture NurOwn without providing data showing the reagent was comparable to the one it previously used.[47]

174. On March 27, 2023, the Company issued a press release informing investors that it

[46] Ex. A, p. 49-51.
[47] Ex. A, p. 16-18.

filed the BLA using the file over protest procedure as well as "filed an amendment to the BLA which responds to most of the outstanding questions the FDA has posed." In an article released the same day in the online publication "Pink Sheet," Defendant Lindborg represented: We have a well-conducted Phase III trial that really, by almost every standard, has operated exactly as planned," she said. "Randomization was very effective. We have a very high completion rate. ***We have fewer deaths than we expected. We have a very strong safety profile."*** Lindborg failed to disclose that there were over three times the number of deaths in the Phase 3 Trial's treatment arm compared to placebo, a safety red flag that FDA raised to Defendants in February 2021.

175. On Brainstorm's "Business Update Call" to investors the same day, Lindborg gave investors a "high-level overview" of the timeline leading to Brainstorm's decision to file the BLA over protest. Lindborg discussed the Company's January 11, 2023 Type A meeting with FDA. Lindborg represented that FDA presented the Company "with ***multiple options*** to return the BLA to regulatory review" and that filing the BLA over protest not only allowed the Company to "reach an AdComm in the shortest amount of time" but "also enabled us to respond to matters identified by the FDA in its refusal to file letter, through amendments to the existing BLA without having to withdraw and resubmit the application, which would have taken many months. ***So in other words, there was no downside utilizing the File Over Protest pathway***, while any other pathway would have lengthened the timelines and Ad Comm and PDUFA date."

176. On the call, Lindborg stated that the Phase 3 Trial's failure to reach its primary endpoint was "very likely driven by participants who entered the trial with advanced ALS, who fell victim to the floor effect of the ALS functional rating scale." Lindborg again represented, referring to Phase 3 Trial participants with baseline ALSFRS-R scores of 35 or above, that "***a pre-specified subgroup with less advanced ALS, for the primary and secondary endpoints as***

specified in the protocol and analysis plan….there was a larger treatment effect across all endpoints with NurOwn compared to placebo with the statistically significant difference observed on a key endpoint for change from baseline in the ALSFRS-R to week 28 with a p-value of 0.05."

177. Given Defendants' emphasis on the "floor effect" subgroup analyses, analyst David Bautz asked Lindborg: "about the floor effect which you guys have discussed a lot, and clearly it had an impact on the trial results." ***I'm just curious, how FDA feels about the floor effect*, are *they aware of it, are they -- do they understand the impact that it can have on trials, like yours?*"**

178. Defendant Lindborg responded, representing that ***"the FDA has certainly seen this data and clearly and has not disagreed with the statements we made."*** Lindborg stated: ***"Yes, I think that will become clear at the advisory committee meeting.*** We've presented clearly as we can and I think very objectively when you take data points on a, the gold standard scale, the ALS functional rating scale that goes back to zero, the baseline. It's pretty objective to say that we can't measure ongoing decline on these items and as you have an accumulation of this, it creates a problem**, *the FDA certainly has seen this data and clearly and has not disagreed with the statements we've made."***

179. In a March 30, 2023 Brainstorm investor conference call Defendants Lebovitz and Lindborg again downplayed the RTF and represented that through an amendment to the BLA, the Company had "conducted much of the work necessary" to respond to and remediate the CMC deficiencies FDA set forth in RTF letter.

180. With respect to the "File over Protest pathway," Lebovitz stated "***Despite its name, this mechanism is a standard regulatory procedure and is not inherently antagonistic***. In fact, we collaborated constructively with the FDA before the agency provided us with ***several regulatory options*** that would reactivate the BLA in order to allow NurOwn to be discussed as an

ADCOM."

181. With respect to the contents of the RTF Letter, Lebovits chose to "speak about how we plan to address these points," stating:

> …***The RTF letter included one item related to the trial not meeting the standard for substantial evidence of effectiveness or the primary endpoint [Indiscernible] statistical significance and the remaining items related to chemistry manufacturing and controls in short CMC. Given our exemplary record of high quality manufacturing, we have full confidence that will be able to remediate each of these points in a straightforward manner.***
>
> ***In fact, we already have conducted much of the necessary work in a short time frame and submitted an amendment to the BLA on March 7, 2023, which responds to the majority of the manufacturing items raised in the letter. We work to respond to the few remaining manufacturing items is ongoing and would be complete in due time. The remaining items RTF letter and the only item related to our clinical data that will be the focus. That will be the key point of the discussion.***

182. Defendant Lindborg lauded the Company's ability to secure an Advisory Committee Meeting, stating, "securing an AdComm has been central to our strategy, ***because we have a robust and compelling data set*** that will benefit from a deep and thoughtful discussion at this public meeting. ***While our Phase 3 trial NurOwn and ALS did not reach statistical significance on the primary endpoint, we firmly believe that the totality of evidence from the trial will ultimately support approval***."

183. Also on the March 30 call, Lindborg heralded NurOwn's safety in response to an analyst's inquiry:

> **Jason McCarthy**: So the last question briefly, can you just ***talk a little bit about the safety aspects*** of an autologous cell therapy being incredibly safe. I think it goes relatively unnoticed when everyone's focused on efficacy versus other types of therapies? ***And how something that's very safe like this could really impact to the good an ADCOM decision***?

> **Lindborg**: We've summarized that very completely, very thoroughly and certainly that will be summarized at our ADCOM. This is a dimension that the physicians closest to our trial, including our Data Safety Monitoring Board***, have continued to express that there were no safety concerns***, that were existed in the trial or that emerged as a -- from a profile of NurOwn and that safety has been clarified to their complete satisfaction.

184. Defendants continued to tout the Phase 3 Trial as demonstrating efficacy. On a May 15, 2023 investor conference call, Defendant Lindborg stated that: "***A thorough analysis of NurOwn Phase 3 data show evidence of clinically meaningful effectiveness and we are further encouraged by the strong and consistent biomarker data, which are predictive of clinical response to the trial span pathways and important to ALS.***"

185. On the call, Lindborg again pointed to the supposedly pre-specified subgroup of Phase 3 Trial participants not impacted by the floor effect, as well as the biomarker data:

> The process for approval of any BLA will be determined primarily by the body of evidence generated. ***And on this front, we firmly believe that NurOwn's data package is strong enough to support regulatory approval***…As disclosed previously, the Phase 3 trial did not reach statistical significance on the primary and secondary endpoints***. However, in a pre-specified group of participants with less advanced disease at baseline, there was a clinically meaningful treatment response on the primary and secondary endpoints with NurOwn compared to placebo***. ***On the secondary endpoint, which was favored by the FDA, the average change from baseline to week 28 and the ALS functional rating scale, the treatment difference was statistically significant at the level of P> 0.05. These findings are important as looking at this pre-specified subgroup enabled us to focus on data that is not as impacted by the floor effect in the scale***….
>
> …So in summary, we can objectively show that the ALS functional rating scale was unable to measure ongoing decline in participants with the most advanced ALS who were enrolled in the trial, a unique sample of trial participants relative to other approved products. ***Based on the data, I've just walked you through, we have clinical and biomarker data that demonstrate evidence of significantly better outcomes in participants treated with NurOwn***. And we have amassed efficacy and safety data that we believe supports a positive benefit risk evaluation of NurOwn.

186. During the quarter ended March 31, 2023, Brainstorm sold 1,800,000 shares of Common Stock at an average price of $1.85 per share for gross proceeds of approximately

$3,330,000 pursuant to an ATM.

187. Then, on June 6, 2023, Brainstorm announced that the FDA planned to convene the Advisory Committee meeting to review the BLA on September 27, 2023, which meant that if FDA approved NurOwn, the Company could begin marketing it in December of that year.

188. Leading up the AdComm Meeting, Defendants reiterated that the Phase 3 Trial demonstrated statistically significant results "once you're able to eliminate advanced patients" and that data from a "new analysis" of the Phase 3 Trial's biomarker results supported NurOwn's "clinically meaningful effectiveness." For example, in an August 14, 2023 Press Release Defendant Lindborg represented that the Company "recently delivered an important presentation…***The data from this new analysis showed that treatment with NurOwn significantly elevated markers of neuroprotection and lowered markers of neuroinflammation and neurodegeneration, including neurofilament light (NfL). Reductions in plasma NfL are believed to be a predictor of clinical benefit in ALS."***

189. In an investor conference call the same day, Defendant Lebovitz responded to analysts' questions concerning the upcoming AdComm, stating: ***"But when you're able to eliminate the advanced patients, we see both in the primary and secondary endpoints, statistical[ly] significant results. Of course, we're not going to lay it out here. That's what we're going to do at the ADCOM."***

190. On July 19, 2023, Brainstorm entered into a securities purchase agreement to sell 4,054,005 shares of Common Stock and warrants at $1.85 per share for gross proceeds of approximately $7.5 million.

V. Defendants Announce the Result of the AdComm and FDA Releases the Briefing Document Exposing Defendants' Prior Misstatements

191. On September 25, 2023, ahead of the FDA Advisory Committee, FDA released the

Briefing Document. On September 27, 2023 the Advisory Committee meeting took place, as planned. The Advisory Committee Members voted 17:1 against FDA approval of NurOwn.

192. Defendant Lindborg represented the Company at the AdComm Meeting. Lindborg herself admitted at the Meeting, when asked about CMC deficiencies, "***we acknowledge that additional works needs to be done and complete to fully satisfy the FDA requirements***."

193. Upon release of the FDA Briefing Document Brainstorm common stock fell $0.39/share, or 48% from its closing price of $0.82 on September 22, 2023 (the previous trading day), to close at $0.43 on September 25, 2023, damaging investors.

194. News of the AdComm Meeting results two days later caused the Company's stock price to decline further, by another 48.72%, or $0.19 per share, to close at $0.20 per share on September 28, 2023.

195. The contents of the FDA Briefing Document and the transcript of the AdComm Meeting directly contradict Defendants' prior representations concerning: 1) the contents of the RTF, 2) NurOwn's safety, 3) FDA's interactions with the Company and the Phase 3 Trial's design, 4) NurOwn's efficacy as purportedly demonstrated by the Phase 3 Trial's results, and 5) NurOwn's prospects for FDA approval.

196. With respect to the RTF, the Briefing Document and AdComm transcript revealed:

> ***On initial receipt of the BLA, FDA determined that the submission was scientifically incomplete to demonstrate substantial evidence of effectiveness, and that the manufacturing information was grossly deficient to ensure adequate product quality. Examples of critical information not provided in the BLA submission include missing or inadequate control of materials, validation of methods missing or incomplete, lack of data demonstrating manufacturing consistency, control strategy for prefilled syringe not provided, inadequate manufacturing and testing facility information, and facilities not ready for inspection.*** FDA therefore refused to file the submission and detailed these deficiencies in a Refuse to File (RTF) letter to the Applicant. The Applicant elected to request that the BLA to be filed over protest, and subsequently provided further

***retrospective* analyses and biomarker results**.[48]

***

…[T]he BLA did not contain information on ***numerous critical elements*** of product manufacturing, and FDA determined that a substantive review was not possible. ***The extent of the deficient information, that facilities were not ready to manufacture the product, and the fact that some clinical validation studies had yet to be initiated, suggested that the best path forward would be to submit a new BLA.***[49]

197. Further, the Briefing Document confirmed that the Company had not remedied FDA's manufacturing concerns, contrary to Defendants' prior assurances:

In addition to the above clinical and statistical concerns, the review team has ***substantial concerns about product manufacturing***. ***Those issues have yet to be resolved***."[50]

198. With respect to safety, the Briefing Document revealed, for the first time:

Survival in the Phase 3 study was worse at study completion for subjects who received [NurOwn]. A total of 13 deaths occurred during the post-treatment follow up with 10 deaths in the [NurOwn] group and 3 deaths in the placebo group; [51]

***

Particularly concerning was the larger number of deaths in the [NurOwn] group compared to the placebo group…[52]

***

Survival is the ultimate clinically meaningful outcome measure for a fatal disease like ALS. It is less likely to be affected by variations in assessment."[53]

***

[48] Ex. A, p. 6.
[49] Ex. B, p. 23.
[50] Ex. A, p. 9.
[51] Ex. A, p. 7.
[52] *Id.* p. 32.
[53] *Id.* p. 50.

> TABLE 4 Safety Summary: ***The [NurOwn] group had higher numbers of life-threatening SAEs[54] and SAEs with fatal outcomes*** compared with the placebo group.[55]
>
> Safety Summary: (1) ***the higher incidence of deaths in the [NurOwn] subgroup with indicates lack of survival benefit of [NurOwn] and warrants further investigation***; (2) there appears to be a ***higher incidence of respiratory failure and dysphagia*** in the [NurOwn] group; (3) there appears to be a ***higher incidence of pain*** (e.g. coccydynia and back pain) in the [NurOwn] group."[56]

199. AdComm member Dr. Gumei Lui, from FDA's office of Clinical Evaluation voiced concerns over the Phase 3 Trial's alarming safety signals, the risks of which were even more pernicious given NurOwn's complete absence of treatment benefit:

> ***During the study, there were more deaths in the MSC-NTF group than in the placebo group…***In addition, MSC-NTF patients experienced a ***higher frequency of pain, such as back pain, musculoskeletal pain, and coccydynia, which would negatively impact the quality of life, especially considering that there was no treatment benefit***. Muscle spasms and dysphagia also appeared to have occurred more frequently in the MSC-NTF group, ***which may suggest continued disease progression in MSC-NTF treated patients***.[57]
>
> ***….We would like to emphasize that this is not a case where an investigational product demonstrates a clear, consistent, and favorable trend, but it just misses the bar for statistical significance. Rather, as shown here, for MSC-NTF, there is no such trend. Furthermore, all-cause mortality, shown in the bottom row, was much higher in MSC-NTF group, with ten deaths by week 28, compared to three deaths in the placebo group.[58]***

200. With respect to the Phase 3 Trial design and the Company's interactions with FDA, the Briefing Document and AdComm Meeting Minutes revealed, for the first time that:

> ***The primary efficacy endpoint of the Phase III study was based on comparing the ALSFRS-R linear regression slope before and after treatment…. FDA and applicant did not reach agreement on the primary efficacy endpoint for the Phase***

[54] Serious Adverse Events
[55] *Id.*
[56] *Id.* p. 51.
[57] Ex. B, p. 120.
[58] *Id.* p. 118-19.

III study[59]

***

Change in 'slope' of ALSFRS-R is of unclear clinical significance, and therefore would not be suitable as the primary efficacy endpoint in a study intended to provide primary evidence of effectiveness in support of a marketing application. As discussed earlier, modeling ALS progression as a linear function based on change in ALSFRS-R over time is inaccurate, because short intervals of plateau or even improvement are not uncommon. ***Moreover, an acceptable clinical outcome measure should reflect whether a patient feels better or survives longer. A change of 1 point or more in the ALSFRS-R total score compared to a patient's baseline corresponds to a clinically meaningful difference in functional ability; in contrast, the clinical meaningfulness of a change in the slope of the regression line is unknown***."[60]

***

The Phase Two study failed to show a statistically significant benefit of MSC-NTF for treatment of ALS. However, the applicant conducted an exploratory subgroup analysis of rapid progressors versus slow progressors. The applicant defined rapid progress as patients with at least two points declined from screening to baseline in approximately three months in their ALSFRS-R total score. The applicant defined slow progress as patients with less than two points declined from screening to baseline in their ALSFRS-R total score. ***FDA communicated to the applicant concerns about the definition of rapid progressors and the exploratory nature of the subgroup findings. However, for the Phase Three study, the applicant then selected only patients who appear to be rapid progressors. Phase Three study also failed to demonstrate a treatment benefit of MSC-NTF on any of the pre-specified primary and secondary efficacy endpoints.***[61]

201. As CBER Statistical Reviewer Dr. Xue Mary Lin explained at the AdComm Meeting, Defendants' failure to follow FDA's advice concerning the Study's design enabled the Company to manipulate the Phase 3 Trial in a way that would generate misleading, false positive results to support a claim of efficacy:

[NurOwn] showed no efficacy compared to placebo on primary and all key secondary endpoints in the overall population. BCT-002-US [The Phase 3 Study] was a failed study. The applicant then tried to rescue the failed study by exploring

[59] Ex. B, p. 118-119.
[60] Ex. A, p. 15.
[61] Ex. A, p. 21-2.

> ***various subgroups.*** ***However, we reiterate the statistical principle that exploratory and post hoc subgroup analysis cannot provide substantial evidence of effectiveness to support regulatory approval because such analysis has a high risk of obtaining false positive results.***[62]

202. Further, the FDA Briefing Document revealed that the Phase 3 Trial's subgroup analyses focusing on floor effect ***were not prespecified***:

> The following subgroup analyses were performed: 1) Subjects with duration since onset of symptoms <1.5 versus ≥1.5 years; 2***) Subjects with baseline ALSFRS-R Score <35 versus ≥35***; 3) Riluzole use; 4) Sex (male versus female); 5) Race (White versus Black or African American). The Applicant also performed analyses on additional subgroups including age group <55 versus ≥55 years, and site of ALS onset: limb or limb and bulbar.
>
> ***The Applicant states that these sub-group analyses were "pre-specified." However, it is important to note that these subgroup analyses were not prespecified for hypothesis testing and no prespecified multiplicity adjustment strategy was employed. Subgroup tests following overall nonsignificant tests in the population as a whole such as the Phase 3 study can only be considered exploratory and hypothesis- generating and do not constitute evidence of effectiveness to support marketing approval of MSC-NTF***.
>
> Data from exploratory subgroup analyses of primary endpoint suggested possible benefit for MSC-NTF recipients in two subgroups: male subjects with ALS, and subjects with ALS with baseline ALSFRS-R ≥35***….[T]he Applicant considers the findings in subjects with ALS with baseline ALSFRS-R ≥35 as evidence of effectiveness. FDA considers that findings from both subgroup analyses could be spurious, as is often the case for such exploratory subgroup analyses***. The Applicant may conduct additional well-controlled clinical study(ies) in subjects with high baseline ALSFRS-R to assess the efficacy and safety of MSC-NTF; ***however, exploratory subgroup analysis data from the completed Phase 3 study cannot serve as evidence of effectiveness***.
>
> ***…Prespecification is the cornerstone of reliable regulatory evidence. Without a prespecified multiple hypothesis testing strategy, the subgroup analysis of patients with baseline ALSFRS-R score greater than or equal to 35 is an exploratory analysis***. In the presence of an overall negative trial result, this subgroup analysis may be used to generate a hypothesis for another trial. ***However, they cannot be used to rescue the trial because of a large chance of a false positive finding***.[63]

[62] Ex. B, p. 22-23.
[63] Ex. B, p. 123-26.

203. And finally, with respect to NurOwn's purported efficacy, the Briefing Document and AdComm Meeting Minutes revealed that there was zero evidence to support Defendants' claim that NurOwn demonstrated any clinical benefit or efficacy. Even Defendants' conjecture that the Phase 3 Trial failed to reach its endpoint because of a "floor effect" was spurious and misleading because no "floor effect" existed given that ALSFRS-R scores of Phase 3 Trial participants in the "floor effect" groups continued to decline:

> The Applicant performed ***three different retrospective analyses on an unblinded, post-hoc subgroup from the Phase 3 study***, excluding in each certain subjects based on the assertion of a 'floor effect' in the ALSFRS-R according to different criteria. A floor effect refers to the insensitivity of an outcome measure to differences at the lower end of an assessment scale. ***In this case, the Applicant claims that a floor effect results in the plateauing of ALSFRS-R total scores over time, during which further deterioration of function cannot be measured. <u>However, no floor effect was demonstrated in the analyses.</u> In addition, floor effect would not be expected in the assessment of survival or biomarkers. Of note, when assessed by change in the ALSFRS-R total score from baseline to Week 28, the MSC-NTF subjects ostensibly affected by a 'floor effect' in fact experienced a numerically larger decline in function over time than did the correspondence placebo subjects***. This result indicated continued deterioration of function and suggests lack of treatment benefit for MSC-NTF subjects.
>
> FDA did not observe a "floor effect" in the floor effect subgroup defined by any of the three definitions identified by the Applicant. ***<u>If there were a "floor effect" in the Applicant-identified floor effect subgroup, the ALSFRS-R total score post baseline would have been bounded by a "floor," which would have prevented the score from much further decline. This is in direct contrast with the fact that the MSC-NTF "floor effect subgroup" had a drastically steeper decline in ALSFRS-R total score from baseline compared with the no floor effect subgroup or the placebo floor effect subgroup.</u>*** At the same time, the magnitude of change between the placebo floor effect subgroup and the placebo no floor effect subgroup were comparable, which further puts into question the validity of the "floor effect" (Figure 12 [using Definition 1] and Figure 14 [using Definition 3]). In addition, the MSC-NTF floor effect subgroup showed substantially worse CAFS ranking than the no floor effect subgroups while the two placebo subgroups were comparable Figure 13.
>
> ***<u>In conclusion, the lack of efficacy of MSC-NTF over placebo cannot be explained by a floor effect</u>***.[64]

[64] Ex. A, p. 37-8.

***

After the fact, analyses by the sponsor found that a subsample of the highest functioning participants of baseline were significantly more responsive to the MSC-NTF than to placebo. Such a post-hoc finding, however, was biased towards a false positive result ***and was invalidated by the FDA review showing that there was no evidence of a sponsored hypothesized floor effect regarding motor function declines from baseline through week 28.*** Laboratory assays and facility inspections have yet to verify the quantity and central nervous system dispersion of cells and trophic factors delivered with each injection….

….***We would like to emphasize that this is not a case where an investigational product demonstrates a clear, consistent, and favorable trend, but it just misses the bar for statistical significance. Rather, as shown here, for MSC-NTF, there is no such trend.***[65]

***

…The applicant has spoken often today of the totality of evidence, including in Dr. Wei's presentation about robustness and consistency. ***But in their presentation totality and consistency of efficacy only apply to the exploratory subgroup analysis. True totality of evidence would include a failure on primary and all key secondary endpoints in the overall study population plus suggestion of survival disadvantage***. This analysis is subject to the same inflated chance of positive findings as the applicant's other exploratory and post hoc subgroup analysis with additional multiple testing issues due to further exploration. ***The p values are uninterpretable***. The permutation test does not protect from uncontrolled type one error inflation associated with post hoc or exploratory testing in any way. ***Methodological papers cited by the applicant do not propose this method be applied to post hoc or exploratory subgroups***.[66]

The applicant's claim of effectiveness relies on subgroup analysis. However, with breaking of randomization, subgroup analyses are subject to bias and incidental findings, and it must always be interpreted with caution…[67]

***

In summary, two randomized, double blind, placebo-controlled studies failed to show efficacy for MSC-NTF. Survival data from the Phase III study were limited and unfavorable. The subgroup analyses can only be considered exploratory. The lack of efficacy in the studies cannot be explained by a floor effect. Biomarker

[65] Ex. B, p. 118-19.
[66] *Id.* p. 123-26.
[67] *Id.* p. 132.

> ***analyses are also exploratory. And the correlation analyses do not support clinical benefit. Finally, product characterization and the manufacturer controls are inadequate***.
>
> ***In conclusion, the totality of data submitted in this BLA does not demonstrate substantial evidence of effectiveness of MSC-NTF for the treatment of ALS or the subgroup of ALS. New, adequate, and well-controlled clinical studies would be needed to provide substantial evidence of effectiveness for the treatment of patients with ALS or for the treatment of patients with mild to moderate ALS***.[68]

204. As to the Phase 3 Trial's biomarker data as supporting efficacy, the Briefing Document and AdComm Meeting Transcript revealed, for the first time, that purportedly positive biomarker data correlated with ***worse*** clinical outcomes, undermining any claim that biomarker data demonstrated a benefit with NurOwn:

> ***The applicant's biomarker analyses were exploratory and did not support clinical benefit***.[69]
>
> ***
>
> Although CSF sampling up to 20 weeks after the first MSC-NTF treatment did identify some biomarkers suggesting that biological drug protects neurons ***these analyses were plagued by missing data in approximately half the sample, and the levels of the biomarkers were mostly not correlated with the functional outcomes***.
>
> ***
>
> ***a reduction in NfL is expected to be associated with reduction in clinical decline of ALSFRS-R total score. However, in the current data set, patients experiencing greater loss of function appears to have a higher reduction of NfL, the opposite of what would be expected.***[70]
>
> ***
>
> ***…I looked at the neurofilament data and I think the FDA presented a very good explanation of the data and why it isn't quite what the sponsor is suggesting….And the relationship between neurofilaments and the efficacy with looking at the ALSFRS-R data that was completely not convincing and I think it***

[68] *Id.* p. 133-34.
[69] *Id.* p. 133.
[70] *Id.* p. 128-29.

> ***was the most random plot that I've ever seen*** that, through which a line was drawn. Anyway, that's how I feel. With regard, again, to Tofersen, they actually found that the neurofilament result dropped already before they saw an improvement. And so, they actually were able to use that as a marker for efficacy. And as I said, that was not just, a five to ten percent decrease, but it was more like a 50 to 70% decrease.[71]

205. Participants at the AdComm Meeting harshly criticized the Company's misleading claims. For example, Dr. Diana Zuckerman, President of the National Center for Health Research and former Yale faculty member, residential director at Harvard, and Bioethics fellow at UPenn stated:

> ***With all due respect, it is not appropriate to combine non-significant results into a significant trend because the more comparisons you make, the more likely one of them would have been statistically significant. But in this case, none of them were. Perhaps most importantly, more patients taking the treatment died. At 28 weeks, 10 of the 95 on the treatment arm had died compared to three deaths of 94 in the placebo group. So, that's more than triple the number of deaths. The Chi-squared analysis is statistically significant. The patients who died during this treatment are not here today, and I want to represent those patients' results, which haven't gotten much attention so far. The improvement at week 28 was the same for the treatment group as the placebo group: 14% improved. This should remind us that some ALS patients will improve even with no treatment. And that's why a controlled trial is so important and why individual success stories, however heartening, can be misleading.***
>
> In conclusion, ***patients deserve clear evidence so that they can make informed decisions. And we all deserve an FDA that approves treatments based on scientific evidence***. Patients should have the option of being in a free clinical trial or expanded access, but ***it would be unconscionable for patients to pay for this unproven treatment, which they would do if the FDA approved it.***[72]

206. Bioethics expert for the FDA AdComm panel Lisa Lee spoke out against Defendants' claims of efficacy as ethically problematic and misleading:

> And I would just like to say that there's absolutely no doubt that ALS is a devastating disease and that there's an urgent need for treatments that are effective. I think we heard from our public commenters, patients and families need hope. ***But providing false hope can be ethically problematic and false hope is provided when the***

[71] *Id.* p. 162-63.
[72] Ex. B, p. 107.

> ***probability of a positive outcome is overestimated. And I think that seems to be the case here creating false hope can be considered a moral injury and the use of statistical magic or manipulation to provide false hope, I think, is problematic both in this current application as well as for the integrity of the drug and device approval process for at large, so I'm worried about what was demonstrated today that might be false hope for persons with ALS or their caretakers and of course, for their loved ones. Several comments that generate false hope that gave me pause today are things like efficacy was shown in four clinical trials, and I don't think the data consistently support this claim or something like the totality of the evidence. It shows efficacy and I think post hoc and biomarker analyses here adding that to the totality of the evidence is mixing evidence with anecdote. And this generates positive outcomes that I believe are overestimated. I think there's no denying that effective treatments are needed, but comments such as 30,000 people with ALS will die while we wait for another trial, these kinds of comments are misleading.***[73]

207. The sole voting patient representative at the AdComm Meeting, Alex Buckley (who suffers from ALS) voted against approval of NurOwn despite the anecdotal evidence some ALS patients provided at the AdComm Meeting, stating:

> ***So, I looked at this through the lens of is this drug safe and is it effective? I didn't find that it was effective. It seemed to me like there's more evidence to the contrary. And then as to the issue of safety, it seems to me it's not as safe as maybe the sponsor would like it to be given the number of deaths in the [NurOwn] group versus the control group.***

208. Less than one month after the AdComm Meeting, the Company held a Business Update Call during which Defendant Lebovitz informed investors that the Company would conduct another trial, this time entering an SPA with FDA, something FDA had urged since as far back as 2016. Lebovitz stated: "***we want to align with the FDA*** on how this is going to be done. ***They want to align with us, which is a very good thing. Maybe even a SPA***. So that's why I want to be careful before throwing [trial] design out."

209. Analysts immediately picked up on the inconsistencies between Lebovitz's above statement and Defendants' prior representations.

[73] Ex. B, p. 181.

Analyst Daniel Walker asked:

> And just lastly, I guess in hindsight ***many investors believed that there was alignment or I guess you had remarked as such various times that there was some alignment with the FDA*** obviously the ADCOM outcome was what it was in terms of looking back at this. Obviously it's early, ***it's only been three weeks, but what would you say is the one sort of key take away from all this…***

Defendant Lebovitz evasively responded:

> ***You ask me, how do we have the strength? But we have a wonderful team***. [ ] .And the FDA asking for [a] trial. So that's great***, not in a position to go into other inside stories within FDA, I don't think that's the right thing for the company to do***. That's great. I appreciate all the answers. Thanks so much.

210. Other analysts were less polite. Analyst Richard Robbins asked:

> Good morning. I have a two-part question. ***First part is Mr. Chairman, you have been the chief architect and the manager of the FDA debacle. Where 17 experts voted against you, One of the participants was even laughing at the data, or at least chuckling at the data. My question to you, Sir, is that given that you were the manager of this, how come you have not resigned? Or why has the board not fired you?***

211. In response, Defendant Lebovitz stated, in part, "I think we did a wonderful outstanding job representing the outcome [of the Phase 3 Trial]…."

212. Exasperated, Robbins remarked:

> ***This, conference call after conference call, I keep hearing that you have confidence in the data yet 17 experts from the FDA- and by the way the FDA holds all the cards, you hold none- did not agree with your data, and in fact one of the participants was even chuckling at the data. Why do you keep saying you have confidence in the data when the FDA doesn't?***

***

DEFENDANTS' FALSE AND MISLEADING STATEMENTS

213. On February 18, 2020 the Company held its Fourth Quarter 2019 Earnings Conference Call. During the call, the Individual Defendants assured investors that the Phase 3 Trial was "aligned with FDA views." Lebovitz gave a "more detailed update on our recent meeting with

the FDA" stating:

> This meeting was very important and was a watershed moment for our ALS development program…Objectives of this meeting were to confirm that there is a clear regulatory path forward for NurOwn and ALS...
>
> ***We had a wonderful discussion. What was most important to Brainstorm was to confirm the data we are collecting in this Phase 3 trial are aligned with current FDA views when considering a BLA for approval***. At the meeting, the FDA confirmed that the full results of Phase 3 trial is collecting relevant data critical to the assessment of NurOwn's efficacy. ***The FDA also commented that this is a well-designed trial***.

214. Lebovitz further represented that Brainstorm could be commercializing NurOwn in 2021, depending on the results of the Phase 3 Trial, stating "***that's why we're so excited that the FDA is having these early conversations about the endpoint, and what they want to gather in the data."***

215. On the call Defendant Kern provided more detail about the FDA meeting, stating:

> The most important outcome of the discussion, of course, was that ***they confirmed we're completing a well-run study***. It is a very high-quality study, and the data that will be collected at the end of this study is relevant and critical to the assessment of NurOwn efficacy. ***It's an important confirmation for us…We obviously were very reassured by their position***."

216. Further, when analyst Jason Kolbert of Dawson James asked Kern about the FDA's views on the Phase 3 Trial endpoint ("***if there was any one single endpoint***, or if you were to focus in on your FDA discussions…"), Kern pointed to the FDA's recent ALS guidance document. Kern stated the recent guidance document was "***one of the reasons why we needed to have a realignment***" and the ALSFRS-R "really forms the foundation for that."

217. The statements referenced in ¶¶213-16 above were materially false and misleading when made and/or omitted material information necessary to make them not misleading because the Phase 3 Trial was ***not*** "aligned with FDA views" and in numerous "conversations about the

endpoint" with FDA, FDA explicitly told Defendants that it disagreed with the Phase 3 Trial's primary endpoint. Defendants knew or recklessly disregarded but failed to disclose that FDA: (i) told Brainstorm, in four separate meetings between 2016 and 2020, that it disagreed with Phase 3 Trial's endpoint because using rate of change in the ALSFRS-R score was "of unclear clinical significance and therefore not suitable as the primary efficacy endpoint in a study intended to provide primary evidence of effectiveness"; (ii) told Brainstorm at the August 7, 2017 meeting and November 18, 2019 meeting that it should obtain an SPA with FDA for a Phase 3 trial to ensure that FDA was aligned with its design; and (iii) told Brainstorm at the November 18, 2019 meeting that it should not enroll only "rapid progressors" in the Phase 3 Study because doing so was based on subgroup results from Brainstorm's Phase 2 study which "are most likely spurious and misleading" and "do not support that your product has any meaningful activity in the treatment of ALS."

218. Then, on November 17, 2020, before the market opened, the Company issued a press release announcing top-line results from the Phase 3 Trial, disclosing that the Trial did not meet statistical significance in its primary efficacy endpoint, but purportedly showed "numerical improvements" in the treatment group, compared to placebo, across primary and secondary efficacy endpoints. On this news, Brainstorm's stock price fell $7.88 per share, or 66% from the previous day's closing price of $11.90/share to close at $4.02.

219. Despite having failed to reach its primary endpoint, Brainstorm represented in the press release that NurOwn demonstrated a "clinically meaningful treatment response" across the primary and key secondary endpoints "in an important ***pre-specified*** subgroup with early disease based on ALSFRS-R baseline score ≤ 35." Brainstorm also stated in the press release that "Cerebrospinal fluid (CSF) biomarker analyses confirmed that treatment with NurOwn resulted in

a statistically significant increase of neurotrophic factors and reduction in neurodegenerative and neuroinflammatory biomarkers that was not observed in the placebo treatment group."

220. In the press release Lebovitz represented: "[t]his clinical trial included a more severely affected ALS population compared to other recent ALS clinical trials. ***We identified a superior treatment response in a pre-specified subgroup of patients with less advanced disease***. We are in active discussions with the FDA who have expressed their eagerness to review the data and have committed to prioritize review of this data."

221. Also on November 17, 2020, Brainstorm filed a form 8-K with the SEC which attached the November 17, 2020 press release as Exhibit 99.1. The Form 8-K was signed by Lebovitz.

222. The above statements in the November 17, 2020 press release were materially false and misleading when made and/or omitted material information necessary to make them not misleading because Defendants knew or recklessly disregarded but failed to disclose that: (i) the subgroup of patients with an ALSFRS-R score of 35 and above was ***not*** prespecified but was instead exploratory, a critical distinction given that "prespecification is the cornerstone of reliable regulatory evidence" and results from post hoc exploratory analysis cannot constitute evidence of effectiveness; (ii) FDA informed the Company at the November 18, 2019 meeting that: 1) it should not only enroll rapid progressors (i.e. "a more severely affected ALS population") in the Phase 3 Trial and 2) subgroup results are "spurious and misleading" and therefore would not be sufficient to support FDA approval and (iii) the Phase 3 Trial's purportedly positive biomarker data corresponded with ***worse*** clinical outcomes: patients with higher reduction of NfL experienced ***greater loss of function***, an entirely unfavorable result that does not support clinical benefit.

223. On February 22, 2021, Brainstorm informed investors in a press release only that

"FDA concluded from their initial review [of the Phase 3 Trial data the Company submitted] that the current level of clinical data does not provide the threshold of substantial evidence that FDA is seeking to support a [BLA]. In addition, FDA advised that this recommendation does not preclude Brainstorm from submitting a BLA submission." The press release stated that Defendants would consult with experts, regulatory advisors, and others before making a final decision as to whether to submit a BLA to FDA.

224. After nearly a year and a half of silence concerning potential submission of a BLA, on August 15, 2022 Brainstorm issued a press release containing its second quarter 2022 financial results and providing a corporate update in which it announced it would in submit a BLA for NurOwn to treat ALS to FDA.

225. The press release represented that a "correction" in the statistical analysis of the data from the Phase 3 Trial resulted in one of the key prespecified secondary endpoints reaching statistical significance. The press release explained that this correction "results in a statistically significant treatment difference of more than two points for an important secondary endpoint, average change from baseline in ALSFRS-R, ***in the prespecified efficacy subgroup of participants with a baseline score of at least 35****….****the newly published results…employ the efficacy model as prespecified in the trial's statistical analysis plan…***"

226. Also on August 15, 2022, Brainstorm filed a form 8-K with the SEC which attached the August 15, 2022 press release as Exhibit 99.1. The Form 8-K was signed by Lebovitz.

227. On an investor conference call the same day, Defendants touted the results from "multiple subgroups" including the Phase 3 Trial's "pre-specified efficacy subgroup" as well as biomarker analyses which purportedly correlated with the "clinical outcomes." Defendant Lebovitz stated:

"While performing routine quality control checks and preparations for upcoming BLA filing, we discovered an error in the statistical model, utilized by a vendor in the analysis of a key secondary endpoint. This is now being corrected... ***Though correcting the error resulted in a change that was relatively small numerically, it does have meaningful positive implications that reinforces and strengthens the conclusions of the Phase 3 study. With the correction, the Phase 3 data are stronger than originally thought as we have achieved statistical significance in a key important secondary endpoints for multiple subgroups, including the trial's pre-specified efficacy subgroup***. The endpoint I'm referring to is average change from baseline to week 28 in ALSFRS-R score in the pre-specified subgroup [of] trial participants with baseline ALSFRS-R scores of at least 35, which is indicative of patients with less disease progression.

228. According to Defendant Lindborg:

Although results showed the trial did not reach statistical significance on the primary or secondary endpoints, ***pre-specified and post hoc analyses showed a larger treatment benefit with NurOwn compared to placebo across both primary and secondary outcomes in patients with less advanced disease***. In addition, data indicate NurOwn had an important effect on a wide range of ***biomarkers*** from all participants in the trial, ***which were shown to be statistically important to the clinical outcomes observed."***

229. Lindborg emphasized the importance of efficacy subgroup analyses in the Phase 3 Trial, supposedly due to the ALSFRS-R floor effect:

I want to offer one other comment regarding the importance of these analyses, which might not be obvious. ***It's common to pre-specify subgroup analyses in large trials in the industry. However, in this trial, efficacy subgroup analyses play an important role in the evaluation of NurOwn's treatment effect because of the higher number of participants enrolled in this clinical trial with advanced ALS at baseline, which is a distinguishing feature of this trial, compared to other registration trials.***

Given the insensitivity of the ALSFRS-R to measure disease progression in these study participants, ***analyses of trial participants less likely to be impacted by the ALSFRS-R floor effect are critical to the evaluation of NurOwn's treatment effect.*** Subgroup analyses are one strategy to do this. To reiterate a point made earlier, we believe these corrected analyses reinforce and strengthen the conclusion from NurOwn's Phase 3 trial.

…When we look at these subgroups that have just been published and when we look at any of the subgroups, [they are] what are allowing us to understand the treatment effect from this trial ***once we've minimized the effect of the lower end of the ALSFRS-R floor effect…***

230. On the call, analyst Daniel Walker drilled down on Defendant Lindborg's

representations concerning ***pre-specified*** secondary endpoints:

> DANIEL WALKER:
>
> And Dr. Lindborg, along those lines, can you please maybe ***just talk a little more about the pre-specified secondary endpoint P-values, and how patients and investors should be thinking about these updated P-values?***
> …So can you maybe just break down the statistics significance of these Phase 3 pre-specified secondary endpoint P-values that met their endpoint? For instance, if you're a patient what should these P-values tell you about NurOwn as a treatment? ***And as an investor, how much confidence should these P-values give you?***

231. In response, Lindborg was careful to emphasize that the subgroup of Phase 3 Trial participants with ALSFRS-R scores of 35 or above was a "***prespecified threshold***" which carries "***a different level of credence.***"

> LINDBORG:
>
> So in terms of pre-specified and our endpoints, our primary and secondary endpoints, it's always really critical that when we're conducting clinical research and this is true in academia, as well as in the industry that we're thinking very carefully about the trial, the questions we want to answer, and then the appropriate ways to analyze the data and really bring forward evidence. ***So your question about pre-specified analyses is important. These were identified before any data was observed in the trial and they therefore give objectivity and a different level of rigor to being able to draw conclusions from the trial. When we look at subgroups, for example, these are also carefully as we focused on the participants that were 35 or above. This was a pre-specified threshold.***
> ***So these analyses carry a different level of credence…***

232. Also on the August 15, 2022 investor conference call, Defendants touted new biomarker analyses from the Phase 3 Trial as supporting efficacy and the BLA submission. Defendant Kern stated:

> I won't give this away today, but what has been true across the board as we work to assess the relationships between biomarker data and clinical endpoints is ***that we consistently see biomarkers that are statistically relevant to clinical endpoints*** covering all these three important ALS pathways. The broad mechanism of action and NurOwn's ability to lower markers of NurOwn inflammation and neurodegeneration in addition to increasing markers of neuro protection all appear to be important in explaining the clinical response that we have observed.

233. Defendant Lindborg echoed that the biomarker data was consistent with improved clinical outcomes, stating:

> "***When we look at our biomarker data and we see changes that were anticipated going in the direction that we expected with NurOwn and stability***, which we also expected with placebo and we see very consistent conclusions across the ranges of the scale, the efficacy scale. That again we're very confident in the scale's ability to measure progression. ***We walk away with a set of data that we believe builds on each analysis and allows us to look at look at the trial results in total.***"

234. The above statements in the August 15, 2022 press release and investor conference call were false and materially misleading because: (i) FDA had already informed the Company at the February 16, 2021 meeting that its "floor effect" analysis was spurious and that the Phase 3 Trial's failure to demonstrate efficacy was *not* due to any supposed floor effects and the data actually demonstrated that NurOwn had a detrimental effect in the floor effect subgroup, directly contradicting Defendants' above claim that analyses of Phase 3 Trial participants less likely to be impacted by the floor effect was "critical" to evaluation of "NurOwn's treatment effect" and giving Defendants no basis on which to assert that the lack of efficacy was due to the subgroup impacted by the floor effect (ii) the subgroup of patients with an ALSFRS-R score of 35 and above was ***not*** prespecified but was instead exploratory, a critical distinction given that "pre-specification is the cornerstone of reliable regulatory evidence" and results from post hoc exploratory analysis cannot constitute evidence of effectiveness and therefore are not "objective" or "carrying a different level of credence"; (iii) the Phase 3 Trial's purportedly positive biomarker data corresponded with *worse* clinical outcomes: patients with higher reduction of NfL experienced *greater loss of function*, an entirely unfavorable result that does not support clinical benefit, (iv) the Phase 3 data was no "stronger" than it was 18 months prior due to a "correction" because it was all based on *post hoc* exploratory analyses that FDA had already invalidated, and (iv) Defendants omitted to disclose

that FDA told the Company at the February 16, 2021 meeting that it was concerned about the larger number of deaths among subjects treated with NurOwn; Defendants also omitted to disclose the deaths themselves.

235. Analyst reports published immediately following Defendants' statements demonstrate that even the most sophisticated analysts were misled by Defendants. For example, on August 15, 2022 analysts Jason McCarthy and Michael Okunewitch at Maxim Group issued a Buy rating stating:

> The company has been continuously analyzing the data from the prior [Phase 3] trial, *including the corrected data around the* ***prespecified*** *analysis of patients with baseline ALSFRS-R score of ≥35 which points to a more robust demonstration of a NurOwn treatment effect.* ***This was based on corrections made the [Phase 3] data publication…The emerging data from the P3 for NurOwn and the announcement of a planned BLA filing are positive for BCLI****."* [while the changes to the data are small] "they push some key secondary measures to [statistically significant] and are clinically important…the results of the proper statistical analysis further support that there seems to be therapeutic benefit for NurOwn in patient with less severe disease particularly for those that fall into ALSFRS-R baseline scores of 35-43. While the changes are small, they are much bigger in our view, when one considers that it pushed the ***key pre-specified measure*** for patients with ALSFRS-R score of at least 35 to [statistically significant]. ***This will also be important for the BLA which is in the process of being finalized for submission***.

236. Similarly, on August 17, 2022 analyst David Bautz from Zacks issued a report giving Brainstorm stock a valuation of $21.00 share, over six times its then-current trading price of $3.44/share based on **"**new clinical analyses of Phase 3 Data."

237. On November 8, 2022 FDA issued the RTF letter to the Company. The RTF letter "detailed all the deficiencies in the BLA submission and provided the FDA's recommendations on how to resolve the deficiencies." In the RTF letter FDA informed Defendants, among other things, that the BLA submission was "***scientifically incomplete to demonstrate substantial evidence of effectiveness, and that the manufacturing information was grossly deficient to ensure product***

quality." "Examples of critical information not provided in the BLA submission include missing or inadequate control materials, validation of methods missing or incomplete, lack of data demonstrating manufacturing consistency, control strategy for prefilled syringe not provided, inadequate testing and facility information, and facilities not ready for inspection."

238. On November 10, 2022, Brainstorm issued a press release informing investors of the RTF. Defendants did not disclose the contents of the RTF, stating the RTF "included *one item* related to the trial not meeting the standard for substantial evidence of effectiveness and Chemistry, Manufacturing and Controls ("CMC") related items."

239. On November 14, 2022 Brainstorm issued a press release announcing the Company's third quarter 2022 financial results and providing a corporate update. The press release announced the Company's request for a Type A meeting with the FDA to "facilitate NurOwn's advancement following receipt of a refusal to file letter regarding the Company's new [BLA]." The press release downplayed the RTF, quoting Lebovitz as stating: "our commitment to ALS patients and our belief in NurOwn's potential to address with unmet medical needs remains unchanged, despite our receipt of a refusal to file letter regarding our new [BLA]." The press release also highlighted additional analyses purportedly showing that "***after controlling for the impact of the ALSFRS-R floor effect, participants treated with NurOwn had a higher rate of clinical response and less function lost across 28 weeks compared to placebo.***"

240. Additionally, the press release also emphasized the "new biomarker data" which "provided further evidence confirming NurOwn's multifaceted mechanism of action."

241. Also on November 14, 2022, Brainstorm filed a form 8-K with the SEC which attached the November 14, 2022 press release as Exhibit 99.1. The Form 8-K was signed by Lebovitz.

242. On an investor conference call the same day, analyst David Bautz asked Defendant Leibovitz: "I'm curious if you could give just a little bit more information about the CMC issues that the FDA brought up? And perhaps importantly, how costly -- if they will be costly, will those changes need to be? Lebovitz responded: "***So the CMC issues are more trivial issues, it's not really costly. It's asking me some questions about some validation, some others, some are already in the BLA, and we have to point out where it is. Some where we anticipate most of the questions, we receive them as review questions. We don't see outside of the clinical comments any red flags.***

243. The above statements in the November 14, 2022 press release and investor conference call were false and materially misleading and/or omitted material information necessary to make them not misleading because: (i) FDA had already invalidated the Company's "floor effect" hypothesis which was based on spurious, post hoc analysis, as set forth in ¶222 above; (ii) the biomarker data did not support NurOwn's mechanism of action and in fact undermined it given that reduction in the key biomarker was associated with worse clinical outcomes; (iii) the CMC issues were not "trivial," instead the FDA informed the Company in the RTF that manufacturing was "grossly deficient" and "critical information" was missing; and (iv) FDA had raised other "red flags," namely there were over three times the number of deaths in the Phase 3 Trial's treatment group compared to placebo and more adverse events which raised serious safety concerns.

244. Defendants' statements misled analysts into believing that the totality of the data pointed to "therapeutic impact," "continued safety," and that the CMC deficiencies "can be easily corrected."

245. For example, immediately following the Company's Nov 14, 2022 press release and

investor conference call, Maxim analyst Jason McCarthy issued a report reiterating a Buy rating for Brainstorm, stating that despite the RTF "NurOwn did have positive signals of efficacy, *and one was recently highlighted* ***with the new biomarker analyses*** *presented at the ALS One Research Symposium on 10/7/2022.* ***The totality of the data points to therapeutic impact and continued safety****…Brainstorm will have a type A meeting with the FDA and discuss the potential to get an Advisory Committee (AdComm) meeting. Overall there seems to be a path forward."*

246. Similarly, on Nov 17, 2022, David Bautz at Zack's Small-Cap Research issued an analyst report, stating:

> In announcing the RTF…The Company indicated that there were two issues with the BLA: the clinical and statistics section, in which the FDA stated that it still seeks substantial evidence of efficacy as shown through a statistically significant treatment effect in the primary endpoint, and the chemistry manufacturing and controls (CMC), ***which the company believes can be easily corrected.…The refusal to file letter is disappointing, however it is by no means a dead end***.

247. On March 27, 2023, the Company issued a press release informing investors that it filed the BLA using the "file over protest procedure" as well as "filed an amendment to the BLA which responds to most of the outstanding questions the FDA has posed." In an article released the same in day in the online publication "Pink Sheet[74]," Defendant Lindborg represented: "We have a well-conducted Phase III trial that really, by almost every standard, has operated exactly as planned…Randomization was very effective. We have a very high completion rate. ***We have fewer deaths than we expected. We have a very strong safety profile."***

248. In the article Lindborg is also quoted as touting the results from the purportedly "prespecified group" stating "[w]hen the company looked at a prespecified group of patients with less disease activity at baseline (ASLFRS-R ≥35), ***there was a large treatment effect across all***

[74] Available at: https://pink.citeline.com/PS147942/BrainStorms-ALS-Treatment-NurOwn-Filed-Over-Protest-Will-Get-US-FDA-Panel-Review

endpoints with NurOwn compared to placebo, and a statistically significant difference on a key endpoint, the average change from baseline."

249. The above statements were false and materially misleading when made and omitted to disclose material information necessary to make them not misleading because Lindborg knew or recklessly disregarded but failed to disclose that: (i) NurOwn did not have a strong safety profile" given the larger number of deaths in the Phase 3 Trial's treatment group and higher number of SAE's, which FDA had expressed concern about, (ii) the subgroup of patients with ALSFRS-R scores of 35 and over was not prespecified, (iii) FDA had already told Brainstorm that the "key endpoint" "average change from baseline" was of unclear clinical significance, and (iv) the amendment to the BLA did not "respond to most of the outstanding questions the FDA posed" because the BLA was missing a large amount of manufacturing information and product data, which, "ha[d] yet to be resolved."

250. On Brainstorm's "Business Update Call" to investors also held on March 27, 2023, Defendant Lindborg gave investors a "high-level overview" of the timeline leading to Brainstorm's decision to file the BLA over protest. Lindborg discussed the Company's January 11, 2023 Type A meeting with FDA. Lindborg represented that FDA presented the Company "with ***multiple options*** to return the BLA to regulatory review" and that filing the BLA over protest not only allowed the Company to "reach an AdComm in the shortest amount of time" but "***also enabled us to respond to matters identified by the FDA in its refusal to file letter, through amendments to the existing BLA*** without having to withdraw and resubmit the application, which would have taken many months. ***So in other words, there was no downside utilizing the File Over Protest pathway***, while any other pathway would have lengthened the timelines and Ad Comm and PDUFA date."

251. On the call, Defendant Lindborg stated that the Phase 3 Trial's failure to reach its primary endpoint was "***very likely driven by participants who entered the trial with advanced ALS, who fell victim to the floor effect of the ALS functional rating scale***." Lindborg again represented, referring to Phase 3 Trial participants with baseline ALSFRS-R scores of 35 or above, that in "***a pre-specified subgroup with less advanced ALS, for the primary and secondary endpoints as specified in the protocol and analysis plan…***.there was a larger treatment effect across all endpoints with NurOwn compared to placebo with the statistically significant difference observed on a key endpoint for change from baseline in the ALSFRS-R to week 28 with a p-value of 0.05."

252. Given Defendants' emphasis on the "floor effect" subgroup analyses, analyst David Bautz asked Lindborg:

> about the floor effect which you guys have discussed a lot, and clearly it had an impact on the trial results." ***I'm just curious, how FDA feels about the floor effect,*** **are** ***they aware of it, are they -- do they understand the impact that it can have on trials, like yours?*****"**

253. Defendant Lindborg responded:

> **I think that will become clear at the advisory committee meeting. We've presented clearly as we can and I think very objectively when you take data points on a, the gold standard scale, the ALS functional rating scale that goes back to zero, the baseline. It's pretty objective to say that we can't measure ongoing decline on these items and as you have an accumulation of this, it creates a problem, *the FDA certainly has seen this data and clearly and has not disagreed with the statements we've made."***

254. The above statements in Brainstorm's March 27, 2023 conference call were false and materially misleading when made and/or omitted to disclose material information necessary to make them not misleading for the reasons stated in ¶222 above and because Lindborg knew or recklessly disregarded but failed to disclose that: (i) at the January 11, 2023 meeting FDA did not

present Brainstorm with "multiple options," instead it gave Brainstorm 2 options, *i.e.*, "address these clinical and product issues and submit a new BLA that contains evidence of effectiveness and evidence of safety from new adequate and well-controlled clinical investigations" or request that the BLA be filed over protest; (ii) the Phase 3 Trial's failure to demonstrate efficacy was not "driven by participants…who fell victim to the floor effect" because at the January 11, 2023 meeting FDA informed Brainstorm that the lack of efficacy could not be explained by a floor effect; (iii) relatedly, the subgroup of trial participants with ALS scores of 35 and above were not "prespecified"; and (iv) FDA had indeed disagreed with the statements Brainstorm made concerning ALSFRS-R floor effects because, in February 2021 FDA told Brainstorm that its "suggested floor-effect did not appear to be consistent across the study population."

255. Defendants' statements continued to mislead analysts into believing that biomarker data and accounting for the floor-effect in a "pre-specified" subgroup demonstrated that NurOwn showed evidence of efficacy in the Phase 3 Trial. On March 28, 2023 in a Maxim Group Equity Research Update, analysts Jason McCarthy and Michael Okunewitch wrote:

> The P3 study missed its primary endpoint of ALSFRS-R, ***however deeper analyses unveiled a treatment effect and impact on key biomarkers, as well as a 'floor effect'*** that may have impacted the ability of the ALSFRS-R scale to capture changes in function.
>
> There are multiple aspects to the NurOwn P3 trial that need to be considered as the trial missed on the primary and Brainstorm received a refuse to file letter in November 2022. ***However, there are multiple positive aspects to the data presented in the top-line and publication that should be considered (shown below) and formed the basis of a meeting with FDA that, as announced on 3/27/23 has led the FDA agreeing to have an Advisory Committee Meeting (AdCom) to discuss the NurOwn BLA.***
>
> ***As noted above, while this trial missed on its primary endpoint in ALSFRS-R change from baseline, for the total population in the study there were positive cuts of the data that demonstrate a clear therapeutic benefit….***
>
> ***There was a pre-specified subgroup with baseline score of at least 35, which is***

> ***more in line with other drugs, yet still below them. The ALSFRS-R scale is challenging to use when it is trying to measure function in patients with very severe disease, low function status. This introduces a 'floor effect' where the ALSFRS-R scale cannot capture changes in patients at the bottom of the scale.***
>
> ***…The totality of the data for NurOwn's P3 study points to a 'floor effect' for about 23% of the total study***. In addition, the mean ALSFRS-R score for the study is below that of comps in the space, and still, ***there seems to be a clear therapeutic benefit***, particularly in patients with less advanced disease.

256. On March 30, 2023 Brainstorm held its Fourth Quarter 2022 Earnings Call. During the call Defendants Lebovitz and Lindborg again downplayed the RTF and represented that through an amendment to the BLA, the Company had "conducted much of the work necessary" to respond to and remediate the CMC deficiencies FDA set forth in RTF letter.

257. With respect to the "File over Protest pathway," Lebovitz stated "***Despite its name, this mechanism is a standard regulatory procedure and is not inherently antagonistic***. In fact, we collaborated constructively with the FDA before the agency provided us with ***several regulatory options*** that would reactivate the BLA in order to allow NurOwn to be discussed as an ADCOM."

258. The above statement was false and materially misleading when made and omitted to disclose material facts necessary to make it not misleading, because in describing the file over protest as "standard and "not inherently antagonistic" Lebovitz provided investors with an overly optimistic picture of NurOwn's prospects for FDA approval while omitting the information contained in the RTF and the Company's regulatory history with FDA concerning the Phase 3 Trial and the BLA. Further, FDA did not provide Brainstorm with "several regulatory options," but only two, *i.e.*, "address these clinical and product issues and submit a new BLA that contains evidence of effectiveness and evidence of safety from new adequate and well-controlled clinical investigations" or request that the BLA be filed over protest.

259. On the March 30 call, referring to the RTF Letter Lebovits chose to "speak about how we plan to address these points," stating:

> …***The RTF letter included one item related to the trial not meeting the standard for substantial evidence of effectiveness or the primary endpoint [Indiscernible] statistical significance and the remaining items related to chemistry manufacturing and controls in short CMC. Given our exemplary record of high quality manufacturing, we have full confidence that will be able to remediate each of these points in a straightforward manner.***
>
> ***In fact, we already have conducted much of the necessary work in a short time frame and submitted an amendment to the BLA on March 7, 2023, which responds to the majority of the manufacturing items raised in the letter. We work to respond to the few remaining manufacturing items is ongoing and would be complete in due time. The remaining items RTF letter and the only item related to our clinical data that will be the focus. That will be the key point of the discussion.***

260. Lebovitz's above statement was false and materially misleading when made and omitted to disclose material facts necessary to make it not misleading because Lebovits knew or recklessly disregarded but failed to disclose that Brainstorm did not have an "exemplary record of high quality manufacturing" and had not "respond[ed] to the majority of the manufacturing items raised in the letter, because the BLA was missing a large amount of manufacturing information and product data. First, the Company failed to assess, and demonstrate in the BLA, as required, that the product administered was comparable across the studies used to support the BLA and did not even show that the product was comparable in the two different sites that manufactured NurOwn administered in the Phase 3 Trial. Second, the Company did not show that it controlled variability of the product for the Phase 3 Trial. Third, the Company did not validate the product's production process, which is necessary to show that the manufacturing process is consistent. Fourth, one quarter of the doses administered in the Phase 3 Trial did not meet the intended dose requirements. Fifth, the level of NTF production, (i.e., the levels of neurotrophic factors normally produced by MSC to

generate NurOwn) was highly variable across the product lots. Sixth, the Company claimed that NurOwn's mechanism of action involved secretion of molecules other than NTF but gave no manufacturing control strategy for any other purported mechanism of action. Relatedly, the Company's proposed mechanism of action in the BLA was inconsistent across the BLA and unclear. Seventh, the product in pre-filled syringes was not necessarily stable and the Company changed a critical reagent used to manufacture NurOwn without providing data showing the reagent was comparable to the own previously used.

261. Further, Lebovitz's statement that the RTF Letter included "only one item related to our clinical data" provided investors with a misleadingly one-sided impression of FDA's view of the clinical data, *i.e.* that no "floor effect" existed and that a floor effect could not account for lack of efficacy, that the subgroup analyses were exploratory only and not evidence of effectiveness, and that Brainstorm should conduct a new Phase 3 study "this time incorporating Agency input regarding the Study design."

262. Also on the March 30 call, Lindborg heralded NurOwn's safety in response to an analyst's inquiry:

> **[Analyst] Jason McCarthy:**
>
> So the last question briefly, can you just ***talk a little bit about the safety aspects*** of an autologous cell therapy being incredibly safe. I think it goes relatively unnoticed when everyone's focused on efficacy versus other types of therapies? ***And how something that's very safe like this could really impact to the good an ADCOM decision***?
>
> **Lindborg:**
>
> We've summarized that very completely, very thoroughly and certainly that will be summarized at our ADCOM. This is a dimension that the physician's closest to our trial, including our Data Safety Monitoring Board***, have continued to express that***

> ***there were no safety concerns***, that were existed in the trial or that emerged as a -- from a profile of NurOwn and that safety has been clarified to their complete satisfaction.

263. The foregoing statement was false and materially misleading when made and omitted to disclose material information necessary to make it not misleading because Lindborg knew or recklessly disregarded but failed to disclose that FDA had expressed concerns about NurOwn's safety and the Phase 3 Trial showed an over threefold incidence of death in the NurOwn group, which shows a lack of survival benefit with NurOwn (at the very least), a higher incidence of SAE's, a higher incidence of respiratory failure and difficulty swallowing, and a higher incidence of pain. This omitted safety information was highly material given that "survival is the ultimate clinically meaningful outcome measure for a fatal disease like ALS [and is] less likely to be affected by variations in assessment."

264. On May 15, 2023 the Company held its first quarter 2023 earnings call. On the call Lindborg stated that: "***[a] thorough analysis of NurOwn Phase 3 data show evidence of clinically meaningful effectiveness and we are further encouraged by the strong and consistent biomarker data, which are predictive of clinical response to the trial span pathways and important to ALS.***"

265. Lindborg again pointed to the supposedly pre-specified subgroup of Phase 3 Trial participants not impacted by the floor effect, as well as the biomarker data:

> The process for approval of any BLA will be determined primarily by the body of evidence generated. ***And on this front, we firmly believe that NurOwn's data package is strong enough to support regulatory approval***…As disclosed previously, the Phase 3 trial did not reach statistical significance on the primary and secondary endpoints***. However, in a pre-specified group of participants with less advanced disease at baseline, there was a clinically meaningful treatment response on the primary and secondary endpoints with NurOwn compared to placebo. On the secondary endpoint, which was favored by the FDA, the average change from baseline to week 28 and the ALS functional rating scale, the treatment difference was statistically significant at the level of P> 0.05. These findings are important as looking at this pre-specified subgroup enabled us to***

focus on data that is not as impacted by the floor effect in the scale….

> …So in summary, we can objectively show that the ALS functional rating scale was unable to measure ongoing decline in participants with the most advanced ALS who were enrolled in the trial, a unique sample of trial participants relative to other approved products. ***Based on the data, I've just walked you through, we have clinical and biomarker data that demonstrate evidence of significantly better outcomes in participants treated with NurOwn***. And we have amassed efficacy and safety data that we believe supports a positive benefit risk evaluation of NurOwn.

266. Lindborg's above statements were false and materially misleading when made and omitted to disclose material information necessary to make them not misleading because Lindborg knew or recklessly disregarded but failed to disclose that: (i) the biomarker data did not demonstrate significantly better outcomes because NfL reduction was associated with *worse* clinical outcomes, (ii) the "group of participants with less advanced disease at baseline" was *not* prespecified and thus the "findings" associated with it were not "important" because they were based on *post hoc* analysis biased towards a false positive result, and (iii) FDA told the Company its "floor effect" analysis was spurious, and the Phase 3 Trial data actually demonstrated that NurOwn had a detrimental effect on the floor effect subgroup.

267. Leading up the Advisory Committee Meeting, Defendants continued to reiterate that the Phase 3 Trial demonstrated statistically significant results "once you're able to eliminate advanced patients" and that data from a "new analysis" of the Phase 3 Trial's biomarker results supported NurOwn's "clinically meaningful effectiveness."

268. On August 14, 2023 Brainstorm issued a press release announcing the Company's financial and operating results for the quarter ended June 30, 2023. In the press release Defendant Lindborg represented that the Company "recently delivered an important presentation…***The data from this new analysis showed that treatment with NurOwn significantly elevated markers of neuroprotection and lowered markers of neuroinflammation and neurodegeneration, including***

neurofilament light (NfL). Reductions in plasma NfL are believed to be a predictor of clinical benefit in ALS."

269. The above statement was false and materially misleading when made and omitted to disclose material information necessary to make it not misleading because Lindborg knew or recklessly disregarded but failed to disclose that in the Phase 3 Trial, reductions in NfL corresponded with *worse clinical outcomes:* patients with higher reduction of NfL experienced *greater loss of function*, an entirely unfavorable result does not support clinical benefit.

270. In an investor conference call also on August 14, 2023, Defendant Lebovitz responded to analysts' questions concerning the upcoming AdComm stating: ***"But when you're able to eliminate the advanced patients, we see both in the primary and secondary endpoints, statistical[ly] significant results. Of course, we're not going to lay it out here. That's what we're going to do at the ADCOM"***

271. Defendant Lebovitz's above statement was materially false and misleading when made and/or omitted to disclose material information necessary to make it not misleading because Lebovitz knew or recklessly disregarded that FDA had already told Defendants that its floor effect analyses (*i.e.* what Lebovitz was referring to above in "eliminat[ing] the advanced patients") were deeply flawed and did not constitute evidence of effectiveness or clinical benefit for the reasons explained in ¶222 above.

ADDITIONAL SCIENTER ALLEGATIONS

272. By virtue of Brainstorm's meetings with FDA, Defendants had actual knowledge that FDA: 1) disagreed with the Phase 3 Trial Design, including its primary efficacy endpoint and Brainstorm's decision to enroll only "rapid progressors" in the Phase 3 Trial; 2) disagreed with Brainstorm's suggested "floor effect" and rejected Defendants' explanation that the lack of

efficacy in the Phase 3 Trial could be explained by a "floor effect" instead determining that it was a *post hoc* analysis based on an exploratory subgroup that could be used only for hypothesis generation, not as evidence to support approval, 3) was concerned about the disproportionately large number of deaths in the Phase 3 Trial's treatment group, 4) and would not approve the BLA for NurOwn without demonstration of substantial evidence of effectiveness through adequate and well-controlled studies. Similarly, by virtue of Brainstorm's receipt of the RTF, Defendants had actual knowledge that the CMC deficiencies could not be "easily corrected."

273. Defendants' knowledge (*i.e.* scienter) of Brainstorm's communications with FDA concerning the Phase 3 Trial and the BLA can be inferred because these facts were critical to Brainstorm's core operations. Defendants regularly touted Brainstorm's clinical development program of NurOwn for ALS to investors.

274. Defendants scienter can further be inferred because Defendants regularly spoke in detail about communications with FDA regarding the BLA as well as the results of the Phase 2 and Phase 3 Trials, and in some instances referenced having personal attended FDA meetings.

275. Defendants were financially motivated to misrepresent the truth and artificially inflate the market price of Brainstorm stock. Brainstorm desperately needed cash to survive and in its SEC filings throughout the Class Period warned that it required substantial additional funding to continue operations, had a history of losses, and expected to incur losses for the foreseeable future.

276. During the Class Period the Company sold 14,424,277 shares of Brainstorm common stock for proceeds of **$73,285,000** in various at-the-market (ATM) and other offerings as follows:

- On March 6, 2020 Brainstorm entered into and closed a registered direct offering selling **1,250,000** shares of common stock at **$8.00** per share for net proceeds of

$10 million.

- During the quarter ended March 31, 2020 Brainstorm sold **336,487** shares of common stock pursuant to an ATM at an average price of **$5.32** per share, raising gross proceeds of **$1.76 million.**

- During the quarter ended June 30, 2020, Brainstorm sold an aggregate of **1,162,527** shares of Common Stock pursuant to an ATM at an average price of **$6.57** per share, raising gross proceeds of approximately **$7.64 million.**

- During the quarter ended September 30, 2020, Brainstorm sold an aggregate of **947,627** shares of Common Stock pursuant to an ATM at an average price of **$14.48** per share, raising gross proceeds of approximately **$13.71 million.**

- During the quarter ended December 31, 2020, Brainstorm sold an aggregate of **3,564,385** shares of Common Stock pursuant to an ATM at an average price of **$6.10** per share, raising gross proceeds of approximately $**21.8 million.**

- During the quarter ended March 31, 2021, Brainstorm sold an aggregate of **1,156,897** shares of Common Stock pursuant to an ATM at an average price of **$6.33** per share, raising gross proceeds of approximately **$7.3 million.**

- During the year ended December 31, 2022, Brainstorm sold **152,299** shares of Common Stock for gross proceeds of approximately **$245,000** pursuant to an ATM.

- During the quarter ended March 31, 2023, Brainstorm sold **1,800,000** shares of Common Stock for gross proceeds of approximately **$3,330,000** pursuant to an ATM.

- On July 19, 2023, Brainstorm entered into a securities purchase agreement to sell **4,054,005** shares of Common Stock and warrants at **$1.85** per share for gross proceeds of approximately **$7.5 million.**

277. Defendant Lebovitz's insider sales also support his scienter. As stated in ¶121 *supra,* between July 9, 2020 and July 16, 2020 Lebovits sold 71,753 shares of Brainstorm stock he beneficially owned through AAC Holdings for proceeds of nearly $1 million ($960,632). Lebovits sold these shares at prices of between $12.99 and $13.47 per share. To put this in perspective, at the end of the Class Period Lebovitz's 71,753 shares were worth only $14,350.60, about sixty-seven times less than what he sold them for. These sales were suspicious in timing and

amount: Neither Lebovitz nor AAC Holdings sold any Brainstorm stock in the 12 months before or after these sales, and these sales took place less than eight weeks before the Phase 3 Trial completion date, whose design FDA disagreed with and which Defendants knew had failed.

278. Defendant Kern's resignation supports scienter. Kern's resignation, which took place about one month after the Company received the RTF and one week before the Company's requested Type A meeting with FDA to discuss the RTF and potentially filing over protest, is highly suspicious and indicates that Kern wanted to dissociate himself from the Company. Further, that Defendants told FE1 that Kern was "retiring" when in fact he took another job less than two months later demonstrates Defendants wished to conceal the true reasons Kern resigned as CMO.

279. Defendants' insistence on concealing the RTF, all FDA communications with Brainstorm, and the contents of the BLA and its amendment from Brainstorm employees supports scienter. As FEs 1 and 2 stated, this level of secrecy was unusual given both the size of the Company and the relevance of this information to FE1 and FE2's job positions. Defendants' secrecy indicates that they did not want employees to know about their misrepresentations to investors, and did not want the damaging information in these documents and communications to get out to investors. Further, Defendant Lebovitz's management style supports scienter. As FE3 stated, rather than have the Company's head of Regulatory Affairs communicate with FDA, Lebovitz himself chose to usurp the role of Regulatory Affairs. This enabled Lebovitz to conceal the true nature of the Company's interactions with FDA concerning NurOwn from both investors and Brainstorm's own employees.

LOSS CAUSATION/ECONOMIC LOSS

280. On November 17, 2020, before the market opened, the Company issued a press release announcing top-line results from the Phase 3 Trial, disclosing that the Phase 3 Trial did not

meet statistical significance in its primary efficacy endpoint, although it purportedly showed "numerical improvements" in the treatment group compared to placebo across primary and secondary efficacy endpoints.

281. On the above news partially correcting Defendants' prior misrepresentations, Brainstorm common stock fell $7.88 per share, or 66% from the previous day's closing price of $11.90/share to close at $4.02 on November 17, 2020, damaging investors.

282. On February 22, 2021 prior to the market opening, the Company issued a press release stating that "FDA concluded from their initial review [of the Phase 3 Trial data the Company submitted] that the current level of clinical data does not provide the threshold of substantial evidence that FDA is seeking to support a [BLA]. In addition, FDA advised that this recommendation does not preclude Brainstorm from submitting a BLA submission." The press release stated that Defendants would consult with experts, regulatory advisors, and others before making a final decision as to whether to submit a BLA to FDA.

283. On the above news partially correcting Defendants' prior misrepresentations, Brainstorm common stock fell $2.70/share, a 39% decline, from its closing price of $6.90 on February 19 (the previous trading day) to open at $4.20 on February 23, 2021, damaging investors

284. On November 10, 2022, Brainstorm issued a press release informing investors of the RTF. Defendants did not disclose the contents of the RTF, stating the RTF "included *one item* related to the trial not meeting the standard for substantial evidence of effectiveness and Chemistry, Manufacturing and Controls ("CMC") related items."

285. On the above news partially correcting Defendants' prior misrepresentations Brainstorm common stock fell $1.22 per share, or 42.21%, to close at $1.67 per share on November 10, 2022, damaging investors.

286. On September 25, 2023, ahead of the FDA Advisory Committee, FDA released the Briefing Document exposing the BLA's deficiencies, NurOwn lack of efficacy, and FDA's advice and warnings to the Company dating as far back as 2016, all of which Defendants failed to follow.

287. Upon release of the FDA Briefing Document correcting Defendants' prior misrepresentations, Brainstorm common stock fell $0.39/share, or 48% from its closing price of $0.82 on September 22, 2023 (the previous trading day) to close at $0.43 on September 25, 2023, damaging investors.

288. On September 27, 2023 the FDA Advisory Committee Meeting took place. The Panel's comments underscored the great extent to which Defendants had misled investors for years concerning the Company's interactions with FDA, the Phase 3 Trial's design and purported results, and the BLA and RTF. The same day, the Company issued a press release disclosing that that the FDA AdComm voted 17 to 1 against approval of NurOwn.

289. On the above news Brainstorm common stock fell nearly half, 48.72%, or $0.19 per to close at $0.20 per share on September 28, 2023, damaging investors.

290. As a result of Defendants' wrongful acts and omissions, and the precipitous decline in the market value of the Company's common stock, Investors and other Class Members have suffered significant losses and damages.

INVESTORS' CLASS ACTION ALLEGATIONS

291. Investors bring this action as a class action pursuant to Federal Rule of Civil Procedure 23(a) and (b)(3) on behalf of a class consisting of all persons other than defendants who acquired the Company's securities publicly traded on NASDAQ during the Class Period, and who were damaged thereby (the "Class"). Excluded from the Class are Defendants, the officers and directors of the Company, members of the Individual Defendants' immediate families and

their legal representatives, heirs, successors or assigns and any entity in which Defendants have or had a controlling interest.

292. The members of the Class are so numerous that joinder of all members is impracticable. Throughout the Class Period, the Company's securities were actively traded on NASDAQ. While the exact number of Class members is unknown to Investors at this time and can be ascertained only through appropriate discovery, Investors believe that there are hundreds, if not thousands of members in the proposed Class.

293. Investors' claims are typical of the claims of the members of the Class as all members of the Class are similarly affected by Defendants' wrongful conduct in violation of federal law that is complained of herein.

294. Investors will fairly and adequately protect the interests of the members of the Class and has retained counsel competent and experienced in class and securities litigation. Investors have no interests antagonistic to or in conflict with those of the Class.

295. Common questions of law and fact exist as to all members of the Class and predominate over any questions solely affecting individual members of the Class. Among the questions of law and fact common to the Class are:

- whether the Exchange Act was violated by Defendants' acts as alleged herein;
- whether statements made by Defendants to the investing public during the Class Period misrepresented material facts about the business and financial condition of the Company;
- whether Defendants' public statements to the investing public during the Class Period omitted material facts necessary to make the statements made, in light of the circumstances under which they were made, not misleading;
- whether the Defendants caused the Company to issue false and misleading filings during the Class Period;
- whether Defendants acted knowingly or recklessly in issuing false filings;

- whether the prices of the Company securities during the Class Period were artificially inflated because of the Defendants' conduct complained of herein; and

- whether the members of the Class have sustained damages and, if so, what is the proper measure of damages.

296. A class action is superior to all other available methods for the fair and efficient adjudication of this controversy since joinder of all members is impracticable. Furthermore, as the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation make it impossible for members of the Class to individually redress the wrongs done to them. There will be no difficulty in the management of this action as a class action.

297. Investors will rely, in part, upon the presumption of reliance established by the fraud-on-the-market doctrine in that:

- the Company's shares met the requirements for listing, and were listed and actively traded on NASDAQ, an efficient market;

- as a public issuer, the Company filed periodic public reports;

- the Company regularly communicated with public investors via established market communication mechanisms, including through the regular dissemination of press releases via major newswire services and through other wide-ranging public disclosures, such as communications with the financial press and other similar reporting services;

- the Company's securities were liquid and traded with moderate to heavy volume during the Class Period; and

- the Company was followed by a number of securities analysts employed by major brokerage firms who wrote reports that were widely distributed and publicly available.

298. Based on the foregoing, the market for the Company's securities promptly digested current information regarding the Company from all publicly available sources and reflected such

information in the prices of the shares, and Investors and the members of the Class are entitled to a presumption of reliance upon the integrity of the market.

299. Alternatively, Investors and the members of the Class are entitled to the presumption of reliance established by the Supreme Court in *Affiliated Ute Citizens of the State of Utah v. United States*, 406 U.S. 128 (1972), as Defendants omitted material information in their Class Period statements in violation of a duty to disclose such information as detailed above.

NO SAFE HARBOR

300. The statutory safe harbor provided for forward-looking statements under certain circumstances does not apply to any of the allegedly false statements pleaded in this Complaint. The statements alleged to be false and misleading herein all relate to then-existing facts and conditions. In addition, to the extent certain of the statements alleged to be false may be characterized as forward looking, they were not identified as "forward-looking statements" when made and there were no meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the purportedly forward-looking statements.

301. In the alternative, to the extent that the statutory safe harbor is determined to apply to any forward looking statements pleaded herein, Defendants are liable for those false forward-looking statements because at the time each of those forward-looking statements was made, the speaker had actual knowledge that the forward-looking statement was materially false or misleading, and/or the forward-looking statement was authorized or approved by an executive officer of Mesoblast who knew that the statement was false when made.

COUNT I

For Violations of Section 10(b) And Rule 10b-5 Promulgated Thereunder Against All Defendants

302. Investors repeat and realleges each and every allegation contained above as if fully set forth herein.

303. This Count is asserted against Defendants and is based upon Section 10(b) of the Exchange Act, 15 U.S.C. § 78j(b), and Rule 10b-5 promulgated thereunder by the SEC.

304. During the Class Period, Defendants, individually and in concert, directly or indirectly, disseminated or approved the false statements specified above, which they knew or deliberately disregarded were misleading in that they contained misrepresentations and failed to disclose material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading.

305. Defendants violated §10(b) of the 1934 Act and Rule 10b-5 in that they:

- employed devices, schemes and artifices to defraud;
- made untrue statements of material facts or omitted to state material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading; or
- engaged in acts, practices and a course of business that operated as a fraud or deceit upon Investors and others similarly situated in connection with their purchases of the Company's securities during the Class Period.

306. Defendants acted with scienter in that they knew that the public documents and statements issued or disseminated in the name of the Company were materially false and misleading; knew that such statements or documents would be issued or disseminated to the investing public; and knowingly and substantially participated, or acquiesced in the issuance or

dissemination of such statements or documents as primary violations of the securities laws. These defendants by virtue of their receipt of information reflecting the true facts of the Company, their control over, and/or receipt and/or modification of the Company's allegedly materially misleading statements, and/or their associations with the Company which made them privy to confidential proprietary information concerning the Company, participated in the fraudulent scheme alleged herein.

307. Individual Defendants, who are the senior officers of the Company, had actual knowledge of the material omissions and/or the falsity of the material statements set forth above, and intended to deceive Investors and the other members of the Class, or, in the alternative, acted with reckless disregard for the truth when they failed to ascertain and disclose the true facts in the statements made by them or any other of the Company's personnel to members of the investing public, including Investors and the Class.

308. As a result of the foregoing, the market price of the Company's securities was artificially inflated during the Class Period. In ignorance of the falsity of Defendants' statements, Investors and the other members of the Class relied on the statements described above and/or the integrity of the market price of the Company's securities during the Class Period in purchasing the Company's securities at prices that were artificially inflated as a result of Defendants' false and misleading statements.

309. Had Investors and the other members of the Class been aware that the market price of the Company's securities had been artificially and falsely inflated by Defendants' misleading statements and by the material adverse information which Defendants did not disclose, they would not have purchased the Company's securities at the artificially inflated prices that they did, or at all.

310. As a result of the wrongful conduct alleged herein, Investors and other members of the Class have suffered damages in an amount to be established at trial.

311. By reason of the foregoing, Defendants have violated Section 10(b) of the 1934 Act and Rule 10b-5 promulgated thereunder and are liable to the Investors and the other members of the Class for substantial damages which they suffered in connection with their purchase of the Company's securities during the Class Period.

COUNT II

Violation of Section 10(b) of the Exchange Act For Insider Trading Against Defendants Brainstorm and Lebovitz

312. Lebovits was in possession of material non-public information at the time he sold his shares, including, among others, that: (a) FDA disagreed with the Phase 3 Trial's primary efficacy endpoint; (b) FDA told Brainstorm not to enroll only "rapid progressors" in the Phase 3 Trial because it was based on spurious exploratory subgroup findings; and (c) the Phase 3 Trial design was not aligned with FDA's views.

313. Through its officers and employee, Brainstorm was in possession of non-public information at the time it sold its shares to the public, including, among others, that: (a) FDA disagreed with the Phase 3 Trial's primary efficacy endpoint; (b) FDA told Brainstorm not to enroll only "rapid progressors" in the Phase 3 Trial because it was based on spurious exploratory subgroup findings; (c) the Phase 3 Trial design was not aligned with FDA's views; (d) the Phase 3 Trial's subgroup of patients with ALSFRS-R scores of 35 and over was not prespecified, was exploratory and could not be used to support FDA approval; (e) FDA invalidated Brainstorm's "floor effect" analysis and told Brainstorm lack of efficacy could not be explained by a floor effect; (f) FDA expressed concerns about NurOwn's safety in light of the Phase 3 Trial data; (f) the Phase 3 Trial's biomarker data correlated with a worse clinical efficacy outcome; (g) the RTF

Letter indicated that the BLA was "scientifically incomplete" and "grossly deficient;" and (h) the CMC issued the RTF Letter flagged could not be "easily corrected."

314. Brainstorm and Lebovitz knew such facts were material to investors.

315. As the sellers of over $74 million of stock during the Class Period, Brainstorm and Lebovitz had a duty to either (a) refrain from selling stock, or (b) to disclose the material facts they were aware of, including, among others, that: (a) FDA disagreed with the Phase 3 Trial's design; (b) FDA disagreed with Brainstorm's exploratory subgroup analysis based on the floor effect hypothesis which it used in an attempt to rescue the failed Phase 3 Trial; (c) FDA expressed serious concerns about NurOwn's safety; (d) the RTF Letter raised serious concerns about the BLA which Defendants did not and could not remedy when they resubmitted the BLA.

316. Investors and Class Members purchased Brainstorm shares contemporaneously with Brainstorm's and Lebovitz's sale of shares.

317. Brainstorm and Lebovitz are liable to all persons purchasing Brainstorm shares contemporaneously with their sales of shares.

COUNT III

Violations of Section 20(a) of the Exchange Act Against the Individual Defendants

318. Investors repeat and reallege each and every allegation contained in the foregoing paragraphs as if fully set forth herein.

319. During the Class Period, the Individual Defendants participated in the operation and management of the Company, and conducted and participated, directly and indirectly, in the conduct of the Company's business affairs. Because of their senior positions, they knew the adverse non-public information about the Company's false financial statements.

320. As officers of a publicly owned company, the Individual Defendants had a duty to disseminate accurate and truthful information with respect to the Company's' financial condition and results of operations, and to correct promptly any public statements issued by the Company which had become materially false or misleading.

321. Because of their positions of control and authority as senior officers, the Individual Defendants were able to, and did, control the contents of the various reports, press releases and public filings which the Company disseminated in the marketplace during the Class Period concerning the Company's results of operations. Throughout the Class Period, the Individual Defendants exercised their power and authority to cause the Company to engage in the wrongful acts complained of herein. The Individual Defendants therefore, were "controlling persons" of the Company within the meaning of Section 20(a) of the Exchange Act. In this capacity, they participated in the unlawful conduct alleged which artificially inflated the market price of the Company's securities.

322. By reason of the above conduct, the Individual Defendants are liable pursuant to Section 20(a) of the Exchange Act for the violations committed by the Company.

PRAYER FOR RELIEF

WHEREFORE, Investors demand judgment against Defendants as follows:

A. Determining that the instant action may be maintained as a class action under Rule 23 of the Federal Rules of Civil Procedure, and certifying Investors as the Class representatives;

B. Requiring Defendants to pay damages sustained by Investors and the Class by reason of the acts and transactions alleged herein;

C. Awarding Investors and the other members of the Class prejudgment and post-judgment interest, as well as expert fees and other costs; and

D. Awarding such other and further relief as this Court may deem just and proper.

DEMAND FOR TRIAL BY JURY

Investors hereby demand a trial by jury.

Dated: April 1, 2024

/s/*Sara Fuks*
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